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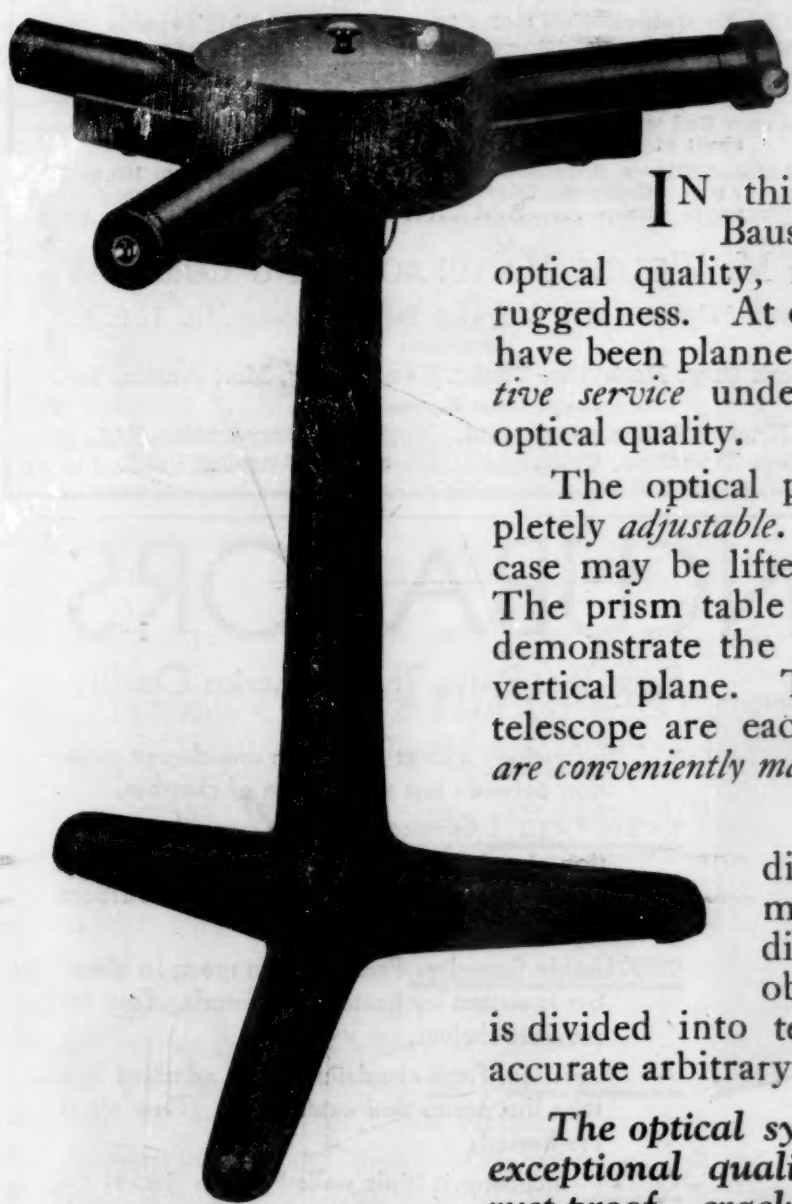
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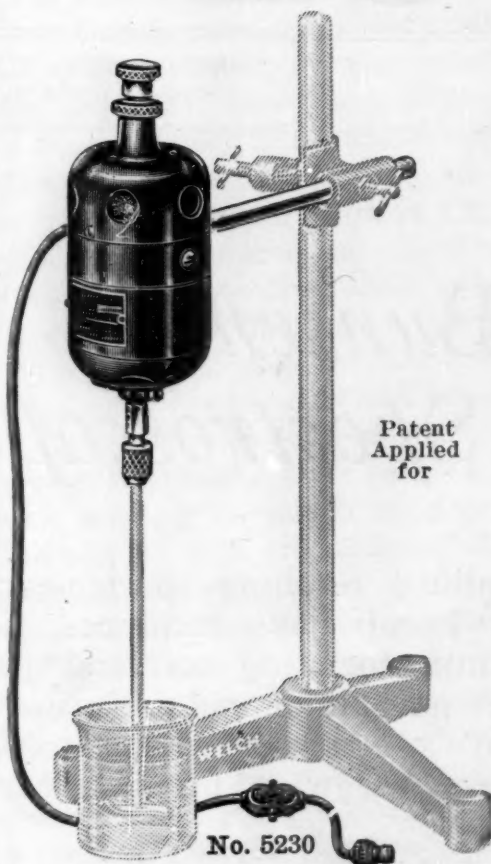
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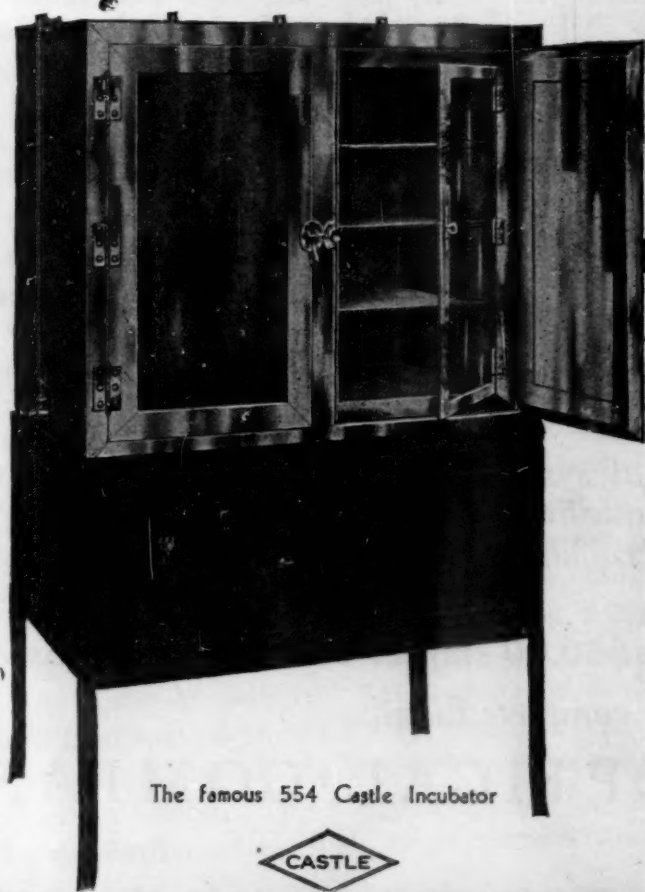
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INFECTION AND RESISTANCE IN THE BLOOD-INHABITING PROTOZOA¹

By WILLIAM H. TALIAFERRO

PROFESSOR OF PARASITOLOGY AND ASSOCIATE DEAN OF THE DIVISION OF BIOLOGICAL SCIENCES, UNIVERSITY OF CHICAGO

CERTAIN of the blood protozoa, because of their size and easily accessible location, offer unique opportunities for the study of the effects of acquired resistance on the parasites and of the humoral and cellular bases for these effects. This evening I propose to discuss two of these in detail, *Trypanosoma lewisi* of the rat and *Plasmodium cathemerium* of the bird, and to consider a few others comparatively. Specifically, I plan to describe the normal course of infection, to analyze the effects of the host's resistance on the parasites, to describe the antibody bases for some of these effects and to correlate the antibody and other immune responses with the cellular reactions

of the host. I sincerely hope that these facts will be of intrinsic interest to you and in addition that they will illustrate the methodology which we have found successful in our immunological studies of protozoan infections. But, above all, I hope that the facts will bring out the peculiar advantages of these protozoa as material for certain immunological problems.

The fundamental methods which we have used in analyzing the effects of resistance will become apparent in the discussion of the specific infections. A few words should be said, however, regarding the method of reproduction in the blood protozoa and the meaning of changes in numbers of the protozoa throughout the course of an infection. Among the trypanosomes reproduction is practically limited to binary

¹Harvey Lecture delivered before the New York Academy of Medicine, December 17, 1931.

fission. In malaria it involves schizogony, which is essentially a series of binary fissions of the nucleus followed by a terminal splitting of the cytoplasm. The organisms in both of these infections are limited to and are distributed throughout the blood stream. Therefore, if no factor or factors influence either the rate of their reproduction or their survival after they are produced, they should increase in the blood uniformly according to a geometrical progression. Conversely, the daily changes in the number of organisms per cmm of blood roughly measure the sum total of the resistance developed by the host, but they do not indicate how much of the resistance is due to an inhibition of reproduction of the parasites and how much is due to a parasitocidal effect which kills the parasites after they are produced. This evening I wish to stress the fact that this inherent difficulty can be overcome by devising various methods of ascertaining the basic rate of reproduction by measures which are independent of the number of organisms killed and the further fact that different immunological mechanisms are involved in the inhibition of reproduction and in the parasitocidal effect.

TRYPANOSOMA LEWISI

It is hardly necessary to recall to your mind that *Trypanosoma lewisi* is a non-pathogenic blood parasite of rats all over the world and is transmitted from rat to rat by various species of fleas. It is a comparatively large trypanosome (about 30 μ in length)

the infection progresses with certain typical features. (See review in Taliaferro, 1929.²) Following the injection of the parasites, unless large numbers have been injected intravenously, there is an incubation period of greater or less time during which no organisms are found in the blood. Then there is an acute rise of the infection until the trypanosomes may reach 300,000 or more per cmm. This peak generally occurs between the 8th and 14th day whereupon the organisms markedly diminish in what I have termed a number crisis. Following this disappearance of most of the parasites the infection enters a developed phase during which there may be a gradual decrease in numbers, but no marked crisis. The developed infection may last from a few days to many months. Sooner or later, however, it is terminated by the more or less abrupt disappearance of the parasites from the peripheral blood stream (Fig. 1). The fact that there is no tissue localization allows certain conclusions to be drawn from these number counts. Undoubtedly there must be a trypanocidal factor killing the trypanosomes at the time of the first number crisis and at the end of the infection to account for the decrease in numbers, since even if the rate of reproduction were reduced to zero, it could not explain an actual decrease of the trypanosomes. The question then arises as to whether in addition to this trypanocidal agent there is also a factor influencing the rate of reproduction.

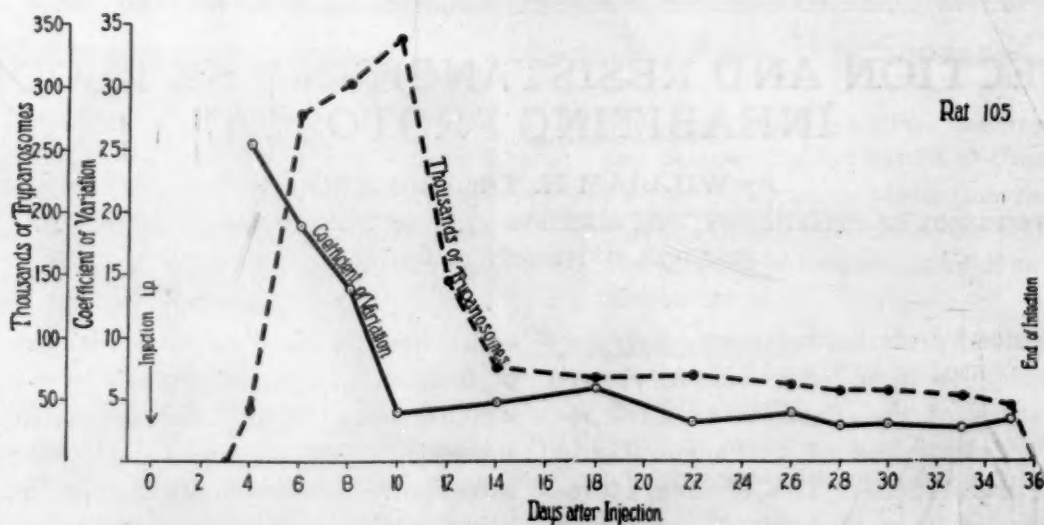


FIG. 1. Graph showing the three factors of resistance developed in a rat against an infection of *T. lewisi*. The two trypanocidal effects are represented by the two crises in the number curve and the reproduction-inhibiting effect is represented by the gradual drop in the coefficient of variation for total length of the trypanosomes. (From the author.)

and occurs in the peripheral blood stream without tissue localization. Thus, what is happening in an infection can be ascertained by a study of samples of the peripheral blood.

Daily number counts of the trypanosomes throughout the course of an infection in the rat show that

A study of the parasites during the ordinary course of an infection indicates that the trypanosomes actually reproduce during only the first part of the infection. Thus, when the trypanosomes are intro-

² W. H. Taliaferro, "The Immunology of Parasitic Infections," New York, pp. 414, 1929.

duced into the rat they begin reproduction by active cell-division within about 48 hours, continue this reproduction at a maximum rate for several days, then at a decreasing rate for several days until approximately the 10th to 12th day of the infection they have ceased to reproduce and live in the blood stream for from a few weeks to many months simply as non-reproducing adults.

As stated in my introductory remarks this inhibition of reproduction is not demonstrated by number counts, but by methods not affected by trypanocidal factors. Two such methods have been devised. The

simplest method consists of ascertaining the percentage of dividing forms found in daily blood smears. Such a procedure (Fig. 2) discloses that actual dividing trypanosomes occur until about the 8th day, that variable growth forms continue until about the 11th day and that only adult forms which are extremely uniform in size and structure and which never show any stages in the division of their organelles are found after the 11th or 12th day. This method of demonstrating the cessation of reproduction in the trypanosomes was known to the early microscopists and the results clearly depicted as early as 1899 by Rabinowitsch and Kempner,³ by v. Wasielewski and Senn (1900),⁴ and especially by Laveran and Mesnil (1901).⁵ A somewhat more exact method was devised by Mrs. Taliaferro and me in 1922⁶ which consists in ascertaining the coefficient of variation for the total length of the trypanosomes throughout the infection. The rationale of this method is based on the obvious fact that reproducing forms with the consequent production of small forms and growth stages are much more variable than non-reproducing adults. Thus, as can be seen in Fig. 1, when the trypanosomes were at the height of their reproductive activity, as demonstrated by microscopical examination, the coefficient of variation for their total lengths was approximately 25 per cent., whereas as they ceased to reproduce, the coefficient of variation proportionately decreased until when the parasites were non-producing adults, it shaded off to about three per cent.

To sum up the effects of resistance on the trypanosomes, we may conclude that there is, first, some factor which completely inhibits all reproduction of the parasites by about the 10th day; second, some trypanocidal factor which kills the majority of the organisms at the time of the first number crisis (8th to 14th day); and third, a similar trypanocidal factor which terminates the infection at the end of a few days to several months.

The next step in analyzing the host's resistance to *T. lewisi* consists in demonstrating that the three effects, just outlined, are connected with definite humoral antibodies. The immunological basis for the inhibition of reproduction of the parasites was first demonstrated by the speaker in 1924⁷ and was later confirmed by Coventry (1925)⁸ and Regendanz and

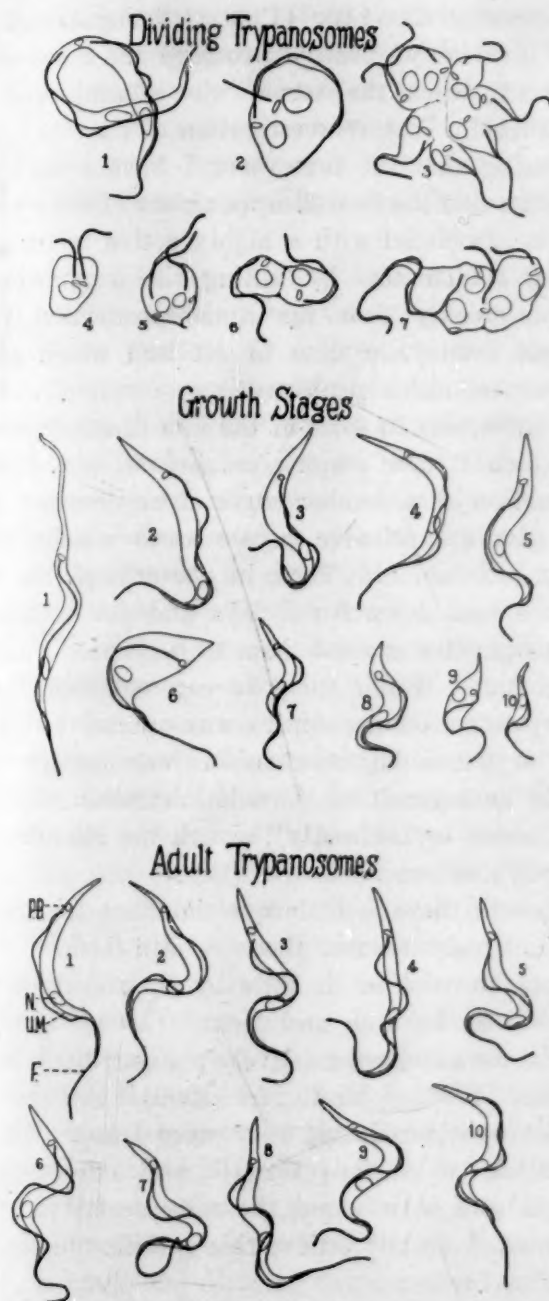


FIG. 2. Dividing, growth, and adult *T. lewisi*. The dividing and growth forms are rarely found after the tenth day of a normal infection. F., flagellum; N., nucleus; P. B., parabasal body; U. M., undulating membrane. $\times 1000$ (Dividing forms, from Coventry; others, from the author.)

³ L. Rabinowitsch and W. Kempner, *Ztschr. f. Hyg. u. Infektionskr.*, 30: 251-294, 1899.

⁴ v. Wasielewski and G. Senn, *Ztschr. f. Hyg. u. Infektionskr.*, 33: 444-472, 1900.

⁵ A. Laveran and F. Mesnil, *Ann. de l'Ist. Pasteur*, 15: 673-714, 1901.

⁶ W. H. Taliaferro and Lucy G. Taliaferro, *Amer. Jour. Hyg.*, 2: 264-319, 1922.

⁷ W. H. Taliaferro, *Jour. Exper. Med.*, 39: 171-190, 1924.

⁸ Frances A. Coventry, *Amer. Jour. Hyg.*, 5: 127-144, 1925.

Kikuth (1927).⁹ Briefly stated, the serum of an infected rat, in which trypanosomes have ceased to reproduce, contains a passively transferable property which will prevent adult trypanosomes from reproducing in normal rats, but which apparently does not kill them or affect their vitality. One experiment will make this clear. On the 10th day after infection (when the trypanosomes had reached the adult stage), a rat was killed and bled and its serum containing adult trypanosomes collected. Next, the trypanosomes were separated from the serum by rapid centrifugation. Then half of the adult trypanosomes together with 2 cc of the serum (per 100 gm rat) were injected into an experimental rat, while the other half of the trypanosomes together with a similar dose of normal rat serum were injected into a control rat. Daily examinations of blood smears and calculations for the coefficient of variation for total length for each of these rats showed that the trypanosomes in the experimental rat lived in the blood for 11 days (when the infection ended) without showing any reproduction whatever, whereas in the control rat reproduction began on the second day and followed the normal course. Moreover, in the experimental rat, the trypanosomes did not increase in numbers, whereas in the control rat, they increased, etc., as usual. In this experiment it is to be noted that not only did the immune rat serum (*i.e.*, the serum taken from the seed rat on the 10th day of its infection) prevent adult trypanosomes from reproducing in a test rat, but normal rat serum failed to prevent adult trypanosomes from reproducing in a control rat. Here, we have a clear-cut passive transfer of this type of immunity from an infected to an uninfected rat.

Similarly, the first number crisis is associated with a trypanocidal antibody as was first demonstrated by Coventry (1930).¹⁰ According to her work, serum taken after the first sudden drop in numbers of parasites, was curative (*i. e.*, caused the trypanosomes to disappear) when injected into rats in which the trypanosomes had just appeared in the blood. Such serum, however, was without effect if injected after the natural number crisis. It appears, therefore, that the parasites that survive the first number crisis are either basically non-susceptible or acquire a resistance to the antibody. Since many observers have shown that whenever a trypanolysin operates on the pathogenic trypanosomes, some of them always survive, become resistant and produce a relapse, it seems not improbable that the non-pathogenic *T. Lewisi*, surviving the action of the trypanocidal antibody at the crisis, becomes similarly resistant.

⁹ P. Regendanz and W. Kikuth, *Centrabl. f. Bakt., Orig.*, 103: 271-279, 1927.

¹⁰ Frances A. Coventry, *Amer. Jour. Hyg.*, 12: 366-380, 1930.

There has been some difference of opinion as to the mechanism whereby the rat eliminates the trypanosomes at the end of the infection. During recent years Regendanz and Kikuth (1927)⁹ concluded that it was the result of a non-specific phagocytosis by the reticulo-endothelial system. On the other hand, a large mass of evidence indicates that it is due in major part to a specific antibody. Thus, as early as 1899, Rabinowitsch and Kempner³ showed that the serum of recovered rats was highly protective (*i.e.*, prevented infection), a fact which was verified and greatly extended by Laveran and Mesnil (1901).⁵ The latter also were able to establish that such serum sometimes, but not invariably, was curative as well. More recently Coventry (1930)¹⁰ demonstrated that it was invariably curative provided the stage of infection at which the serum was administered was standardized. In a reinvestigation of the whole question during the last few years I have come to the conclusion that the final disappearance of the trypanosomes is associated with a highly active trypanocidal antibody which acts by killing the organisms and kills so quickly that the anti-reproduction factor does not even have time to act and which can be demonstrated either protectively or curatively. Some of the infections in some of the rats illustrate another fact which I have emphasized before, *viz.*, that the examination of a number curve alone does not necessarily give a conclusive answer as to whether reproduction is inhibited. Thus, in one animal, the infection was held down for 8 days and yet examination of the parasites showed them to be reproducing at a normal rate. From this, we can conclude that no anti-reproductive mechanism was operative, but that some trypanocidal mechanism was active either directly as a result of the administration of the immune serum or indirectly through the stimulation of the body's defense.

Although there is little question that the trypanocidal antibody occurs, there is still lack of agreement as to whether it kills by opsonization or by lysis. Thus, Laveran and Mesnil (1901)⁵ considered that the parasites were actively phagocytosed, whereas MacNeal (1904),¹¹ Manteufel (1909)¹² and the author (1924)⁷ considered that they were lysed. Since the contention of Wells (1929)¹³ and others that an opsonin and a lysin are the same seems to me well grounded, I do not believe this specific question need worry us further.

I have described in *T. Lewisi* two markedly different effects of resistance, namely, the inhibition of repro-

¹¹ W. J. MacNeal, *Jour. Infect. Dis.*, 1: 517-543, 1904.

¹² Manteufel. *Arb. a. d. k. Gesundh.*, 33: 46-83, 1909.

¹³ H. G. Wells, "The Chemical Aspects of Immunity." 2nd. New York, pp. 286, 1929.

duction and their destruction and have ascribed their action to antibodies. The question arises: Are these antibodies identical? After some seven years' study, I (in press)¹⁴ now feel that they are essentially different. Both antibodies show the following similar characteristics. Both are associated with the activity of the spleen and other locations rich in reticulo-endothelial cells: both are precipitated with the globulin fractions of the serum: both appear in suitable animals after immunization with killed *T. lewisi*: both are specific for *T. lewisi*; and both arise as a result of infection of an animal with *T. lewisi*. They exhibit the following differences. The reproduction-inhibiting antibody inhibits cell-division, but does not kill the parasites or induce them to become resistant, and it shows no persistent union with the trypanosomes *in vitro* so that neither is the property absorbed by the trypanosomes nor are the trypanosomes sensitized against reproduction as tested by washing them free of the serum and injecting them into normal rats.

The lack of *in vitro* affinity between the reproduction-inhibiting antibody and the specific antigen, *i. e.*, *T. lewisi*, is particularly interesting and should be emphasized. It is comparatively easy to show the *in vitro* affinity of *T. lewisi* for its specific trypanocidal antibody. Thus, in a typical experiment, serum, which was obtained after the natural termination of the infection, when tested *in vivo* was trypanocidal in curative experiments in doses of 1.0 cc to 4.0 cc per 100 grams rat and in protective experiments in doses of 2.0 cc to 5.0 cc. After absorption with dividing and adult trypanosomes—about 1,000,000 trypanosomes per cmm—there was no trypanocidal action in curative experiments in doses as high as 4.0 cc nor in protective experiments with one exception, in doses as high as 6.0 cc. The trypanosomes used for this absorption were highly sensitized so that they lived only a few minutes when introduced intravenously into a normal rat. In marked contrast to this, reproduction-inhibiting serum (*i. e.*, serum taken after the inhibition of reproduction, but before the termination of the infection) when tested *in vivo* elicited inhibition of reproduction of trypanosomes in doses of 1.5 cc to 4.0 cc per 100 grams rat, whereas after absorption with dividing trypanosomes its titer was exactly the same. Similar results were obtained when the serum was absorbed with adult trypanosomes and with both adult and dividing trypanosomes. Furthermore, the trypanosomes used in attempting to absorb the serum were not sensitized against reproduction because when injected into normal rats they underwent their usual cycle of reproduction. The objec-

tion might be raised that sufficient trypanosomes had not been used. Two facts militate against such an objection. In the first place, if too few were used those that were used would have been very highly sensitized by the antibody. But they were not. In the second place, I have found it possible to take serum after the termination of the infection which contains both the trypanocidal and the reproduction-inhibiting antibody and by absorption to remove the one and leave the other. In the light of this work and in the interest of a more concise terminology I¹⁴ have just recently designated the principle in serum which inhibits cell-division of organisms but does not kill them as *ablastin*, from the Greek *blastos*, a sprout, germ, offspring and *ablastos*, not budding, barren, etc. Parenthetically I may add that I have always favored the unitarian hypothesis that the various serological manifestations exclusive of antitoxin-toxin reactions, are due to a single antibody. Although the trypanocidal antibody is undoubtedly a manifestation of this single postulated antibody, I believe, that the work just reviewed indicates that the reproduction-inhibiting antibody is essentially different.

As has been previously noted, the reproduction-inhibiting antibody or *ablastin*, is associated with the activity of the spleen and other locations rich in reticulo-endothelial cells. This fact is of inherent interest and has elicited considerable work. In 1927, Regendanz and Kikuth⁹ showed that removal of the spleen of trypanosome-infected rats often caused a lengthening of the reproduction of the trypanosomes which they interpreted as following from a decrease in the formation of this specific antibody. Marmorston-Gottesman, Perla and Vorzimer,^{15, 16, 17} in a series of papers published in 1930, corroborated and extended these findings. These results were somewhat complicated, however, by the fact that both groups of investigators used rats which were infected with *Bartonella muris-ratti*, although the first investigators tried to control the infection with neo-salvarsan. Infection with this organism will remain latent and unnoticed ordinarily, but will flare up with intense anemia upon any pronounced disturbance of the reticulo-endothelial system, such as splenectomy. In other words, infections with both *Bartonella* and *T. lewisi* are intimately connected with the action of the reticulo-endothelial system. Consequently, in collaboration with Cannon and Goodloe, I (1931)¹⁸ re-examined the relationship of the spleen and the gen-

¹⁵ J. Marmorston-Gottesman, D. Perla and J. Vorzimer, *Jour. Exp. Med.*, 52: 587-600, 1930.

¹⁶ J. Marmorston-Gottesman and D. Perla, *Jour. Exp. Med.*, 52: 121-129, 1930.

¹⁷ D. Perla and J. Marmorston-Gottesman, *Jour. Exp. Med.*, 52: 601-616, 1930.

¹⁸ W. H. Taliaferro, P. R. Cannon and Sara Goodloe, *Amer. Jour. Hyg.*, 14: 1-37, 1931.

¹⁴ W. H. Taliaferro, *Amer. Jour. Hyg.* (in press), 1932.

eral macrophage system to the formation of the reproduction-inhibiting antibody in *Bartonella*-free as well as *Bartonella*-infected rats and found that it was demonstrated by histological changes, by splenomegaly and by various experimental procedures known to affect the reticulo-endothelial system. Thus, rats infected with *T. lewisi*, but *Bartonella*-free, showed in the spleen an increased prominence of the follicles and marginal zones, and a mild hyperplasia of both red and white pulp cells. These cellular changes were not as pronounced as those found when *Bartonella* alone was present (Cannon and McClelland, 1929)¹⁹ and were even less pronounced than when *Bartonella* was present in conjunction with *T. lewisi*. Moreover, this work demonstrated that when such things as splenectomy, *Bartonella*-infection, paratyphoid infection, India ink blockade and pregnancy occur separately in a rat infected with *T. lewisi*, the reproductive cycle of the trypanosomes is not materially influenced, but that when two or more occur in conjunction with *T. lewisi* in the same rat, the reproductive activity of the trypanosomes is often profoundly altered. To illustrate—in one rat which was infected with *Bartonella* the trypanosomes underwent their usual cessation of reproduction in the initial infection, but when splenectomy was performed, an intense relapse of reproduction became evident within three days after the operation and during the later stages of pregnancy, a similar relapse occurred.

Taken as a whole, this work indicates that the macrophage system in rats infected with *T. lewisi* but otherwise healthy has an effective functional level so that by the 8th to the 12th day of the infection all reproduction of the trypanosomes is inhibited and continues to be inhibited throughout the remainder of the infection, that this functional level is lowered in a cumulative way by splenectomy, *Bartonella*-infection, paratyphoid infection, India ink blockade and pregnancy, so that any one alone produces no significant derangement, but two or more in combination elicit profound disturbances in a high percentage of rats.

A similar relationship between the reticulo-endothelial system and the trypanocidal antibody in *T. lewisi* can be demonstrated, but I have stressed the relationship between the reticulo-endothelial system and the reproduction-inhibiting antibody because it is so clear-cut and gives such a unique tool for the study of the reticulo-endothelial system, not only in connection with its relation to immune phenomena, but also in establishing its connection with various general metabolic processes. Thus, we hope to infect rats with trypanosomes, wait until their reproduction has ceased and then subject them to various physiological dis-

turbances, such as dietary insufficiencies, hormone administration, fatigue and numerous other factors to see if the trypanosomes reinitiate reproduction. If they do, we feel that we are justified in concluding a direct interrelationship of such physiological factors and the reticulo-endothelial system.

I shall not consider other species of trypanosomes in detail, but certain comparative facts should be brought out. In no case so far studied is the reproduction-inhibiting antibody or ablastin formed in infections with the pathogenic trypanosomes.^{2,6} In fact, that appears to be the outstanding difference between the two groups. Thus, when *T. brucei*, *T. gambiense*, *T. rhodesiense*, *T. equiperdum* and related forms are grown in mice there is no evidence of the action of either trypanocidal or reproduction-inhibiting factors. When the same forms are grown in the guinea-pig no reproduction-inhibiting factor is operative, but periodic trypanolysins are liberated in the blood and are associated with decreases of the parasites. Much the same probably holds for sleeping sickness in man. These trypanolysins are not permanently effective, however, because as a rule all of the trypanosomes are not killed and the survivors become resistant to the antibody. Being resistant and having their basic rate of reproduction unchanged, they repopulate the blood stream in one or more relapses until the animal succumbs.

Ablastin undoubtedly plays an important part in the prevention of relapses. Thus, during the first part of the infection with *T. lewisi*, the reproduction of the parasites is first reduced to zero. Therefore, when a trypanocidal factor appears it permanently reduces the parasites in the blood because those that remain can not reproduce, and hence can not reaccumulate or produce a relapse, as they do in the pathogenic infections. Similar antibodies occur in a group of non-pathogenic trypanosomes closely related to *T. lewisi*, but have not been found in a number of other infections which we have studied.

PLASMODIUM CATHEMERIUM

As a second infection to consider in detail, I have selected the frequently non-lethal malarial parasite, *Plasmodium cathemerium*, of the sparrow which can be experimentally studied in the canary. In this infection, unlike infection with *T. lewisi*, only a parasitocidal type of resistance is developed and furthermore, no intermediate action through a humoral antibody has been demonstrated, although the parasitocidal mechanism is again associated with the macrophage system in what Gay (1931)²⁰ has aptly referred to as a "pure histologic immunity."

The peculiar synchronous method of reproduction

¹⁹ P. R. Cannon and P. H. McClelland, *Arch. Path. and Lab. Med.*, 7: 787-800, 1929.

²⁰ F. P. Gay, *Jour. Amer. Med. Ass.*, 97: 1193-1199, 1931.

found in the malarial parasites allows us to carry our analysis of the factors in resistance somewhat further than in the case of *T. lewisi*. I need only recall to your mind that, whereas reproduction in the trypanosomes is haphazard, in the malarial organisms it is synchronous. Thus, all the young asexual parasites (which are the typically vertebrate part of the life-history of this form) grow up and sporulate more or less simultaneously so that at any one time a preponderance of one particular stage will be found in the blood. In the case of *Plasmodium cathemerium*, according to L. G. Taliaferro (1925)²¹ and others, this asexual cycle takes 24 hours. As shown in Fig. 3,

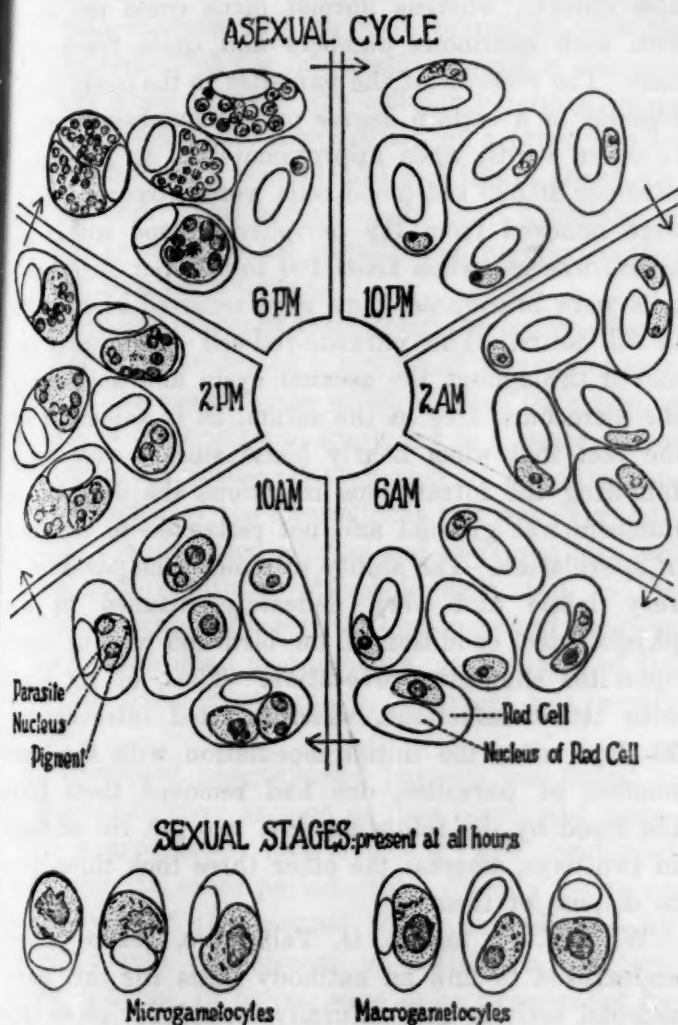


FIG. 3. Outlines of the asexual stages of *P. cathemerium* showing the synchronous method of reproduction occurring every 24 hours. $\times 1350$. (From L. G. Taliaferro.)

the young parasites start their existence about 6 P. M., grow, undergo a series of nuclear divisions and 24 hours later break up, i. e., sporulate, into about 15.5 small parasites. Thus, the mean size of random samples taken throughout the day will show this cycle inasmuch as the mean size is small when there are only merozoites and increases until it reaches a peak just before the mature schizont breaks up dur-

²¹ Lucy G. Taliaferro, *Amer. Jour. Hyg.*, 5: 742-789, 1925.

ing sporulation. From the standpoint of our present study the length of this asexual cycle, which is the time it takes one parasite to become 15, is a direct measure of the rate of reproduction of the parasites since the parasites always segment into approximately the same number, and it is a measure which is independent of parasitocidal factors.

Superficially the course of the infection of *P. cathemerium* in the canary is very similar to *T. lewisi* in the rat. Thus, there is an early acute rise in the number of parasites which reaches its peak between the 8th to the 15th day and which is followed in turn by a sharp number crisis, by a period of developed infection when there are comparatively few parasites in the blood, and by a latent stage which may last for as long as four years and during which there are so few organisms in the blood that they can rarely be found by microscopic examination, but can be demonstrated by injecting large amounts of blood into uninfected birds. Throughout this latent period severe relapses may occur (See the Sergeants, 1918,²² Ben Harel, 1923,²³ L. G. Taliaferro, 1925,²¹ Boyd, 1924²⁴ and Hartman, 1927.²⁵) Just as in *T. lewisi*, there are no tissue localizations so that from the number curve alone we are justified in concluding that some parasitocidal mechanism eliminates most of the parasites at the time of the crisis.

When the rate of reproduction of the organisms is studied, however, we find an entirely different picture from that in *T. lewisi*. L. G. Taliaferro (1925)²¹ found that the rate of reproduction of the parasites remained constant during the acute, chronic and relapse periods. In other words, the parasites reproduced every 24 hours whenever they could be found

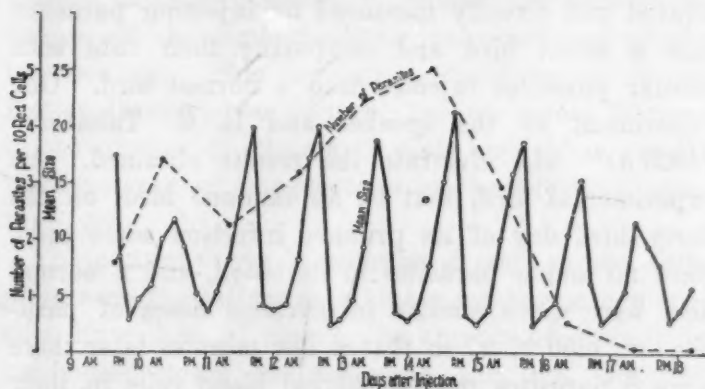


FIG. 4. Graph showing the plasmodicidal factor of resistance developed in a bird against an infection with *P. cathemerium* as represented by the crisis in the number curve. There is no reproduction-inhibiting effect as shown by the regularity of the mean-size curve, i. e., every 24 hours the parasites sporulated. (From L. G. Taliaferro.)

²² Ed. Sergeant and Et. Sergeant, *Ann. de l'Inst. Pasteur*, 32: 382-388, 1918.

²³ S. Ben Harel, *Amer. Jour. Hyg.*, 3: 652-685, 1923.

²⁴ G. H. Boyd, *Amer. Jour. Hyg.*, 5: 818-838, 1925.

²⁵ E. Hartman, *Amer. Jour. Hyg.*, 7: 407-432, 1927.

in the blood for study. Fig. 4 shows the regularity of the mean curve during the major portion of the acute period, the crisis and the beginning of the latent period of an infection. From this it follows that there is no reproduction-inhibiting effect of resistance such as exists in infections with *T. lewisi*.

The parasitocidal effect may now be considered in detail. As was previously indicated, the average number of merozoites formed from one parasite was found to be 15.5 and on *a priori* grounds the daily rate of increase of the parasites during the acute period should be the same. Number counts, however, revealed that the increase was only by 5. In other words, each schizont produced a brood of approximately 15 parasites, but ten of them died before completing their reproductive cycle. This rate of death occurred immediately after the bird was infected and was constant throughout the acute period. It does not, therefore, represent an acquired resistance, but probably is a measure of the suitability of birds for the malaria parasite and represents in a sense a natural immunity. Whether or not it is the result of active processes in the bird, such as specific phagocytosis, or is a natural death rate of the parasites, as suggested by Hartman (1927),²⁵ has not been definitely proven.

At the time of the crisis instead of 10 parasites out of each brood of 15.5 being killed, the rate of death of the parasites was far in excess of the net rate of reproduction. This represents an acquired resistance resulting from infection which is effective to a greater or less extent in holding the parasites down throughout the remainder of the infection.

That it is preeminently efficient has been demonstrated and directly measured by injecting parasites into a latent bird and comparing their fate with similar parasites injected into a normal bird. One experiment by the speaker and L. G. Taliaferro (1929a)²⁶ will illustrate the results obtained. An experimental bird, that is, an immune bird, on the forty-third day of its primary infection when there were no longer parasites in its blood, and a normal bird were given similar intravenous doses of parasites at 1:00 P. M. so that a few minutes later there were 8 parasites per 10,000 red blood cells in their blood. The sequence of events in the two birds was strikingly different. Whereas in the experimental bird the parasites had disappeared by 10:00 A. M. the day after the intravenous injection and never reappeared (the bird died on the eighth day of the experiment), in the control bird they showed a typical course of infection. The results were even more dissimilar when larger doses of parasites were given, for

²⁶ W. H. Taliaferro and Lucy G. Taliaferro, *Jour. Prev. Med.*, 3: 197-208, 1929a.

the immune birds disposed of their parasites so that they could no longer be found 2 to 3 days after injection, whereas the normal birds died between the fifth to eighth day from the ensuing overwhelming infection with approximately every other cell parasitized.

Other conclusions from the same paper may be briefly summarized as follows: There is a high degree of immunity to superinfection which begins as soon as the latent period sets in and lasts for extremely long periods. Thus, birds with latent infections that had been inoculated from 16 to as long as 656 days previously, when superinfected, disposed of the parasites quickly, whereas normal birds could not cope with such enormous numbers and quite frequently died. The removal of the parasites in the latent birds depends to a certain degree on the number injected. In other words, when approximately 1 to 100 parasites per 10,000 red blood cells were introduced, they were removed from the peripheral blood within 24 hours, whereas when from 100 to 400 per 10,000 red cells were introduced, they were removed in from 48 to 76 hours. The parasite-red-cell complex is removed throughout the asexual cycle and not simply the merozoites free in the serum, as is evidenced by the fact that when hourly blood smears were made following the intravenous injections the decrease in numbers was gradual and not restricted to the time of sporulation. The ability to remove the parasites is very labile and very delicately attuned to the physiological condition of the bird and may be upset upon the slightest provocation. Thus, of six birds with latent infections, when injected intravenously 33 days after the initial inoculation with the same number of parasites, one had removed them from the blood by the following day, two got rid of them in two days, whereas the other three took three days to dispose of them.

We (W. H. and L. G. Taliaferro, 1929b)²⁷ then endeavored to find an antibody basis for this parasitocidal activity and naturally looked for some type of antibody similar to the ones easily demonstrated in the trypanosome infections. In this we completely failed. Thus, in six birds which were given varying doses of serum up to 1.05 cc, which is more than the amount obtainable from one bird, the infection showed up within from 1 to 6 days, whereas similar infections in normal birds showed up in from 1 to 9 days. This and other experiments led to the conclusion that immune serum, *i.e.*, serum recovered from birds during a latent malarial infection, was without curative, protective or opsonizing effect on the parasites. Nevertheless, at the close of this talk, I shall

²⁷ W. H. Taliaferro and Lucy G. Taliaferro, *Jour. Prev. Med.*, 3: 209-223, 1929b.

present evidence which still makes me feel that either some type of antibody must be present or the macrophages must be specifically changed.

The absence of an antibody basis for the high grade immunity to superinfection and the subsequent natural recovery from avian malaria made it all the more interesting to study the cellular basis for the effects we have described. This phase of the work has been done in collaboration with Professor P. R. Cannon, of the department of pathology of the University of Chicago (1931).²⁸ A study was made first of normal birds and of the cellular changes occurring in infected birds throughout the course of infection and these changes in turn were correlated with the various periods of the infection. Second, a comparison was made between the cellular reactions immediately following the introduction of a large number of parasites into a normal bird and into a latent, *i.e.*, immune bird. This second study gave a picture of the cellular basis for the parasitocidal mechanism that we have been considering.

The cellular reactions throughout the course of normal infections presented a picture of increasing activation of the mesenchyme which reached its height at the time of the crisis and continued to a lesser degree throughout the entire latent period of the infection. This activation of the mesenchyme was not only indicated by the increased mitoses and increased numbers of the undifferentiated lymphoid cells, but by the heightened phagocytic activity and increased numbers of the differentiated macrophages, particularly of the spleen and liver. Furthermore, the spleen was greatly enlarged.

An occasional phagocytosed parasite was found in the spleen and liver as soon as four hours, and thereafter, phagocytosis was constant and continued throughout the acute period—thus, directly verifying the decrease of the asexual forms as indicated by number counts. Evidences of activation first appeared in about 18 hours, were quite pronounced by 24 hours and then were increasingly apparent until they reached a climax between the eighth and tenth days concomitantly with the crises of the infection. At the time of the crisis, when so many parasites were being swept from the general circulation, the Kupffer cells in the liver were swollen and contained large numbers of malarial organisms and there was a striking increase in mitosis and in the number of mononuclear cells. The liver cords were notably disoriented. Similarly in the spleen there was a larger proportion of pulp cells (macrophages) containing malarial organisms coupled with a diffuse hyperplasia of lymphoid cells and a great increase of basophilic

lymphoid cells. After this high point of activation, there was a gradual decline in phagocytosis and activation. This probably follows from the fact that once the body has gotten the infection in hand, there are comparatively few parasites present for removal. Nevertheless, that the altered reactivity is maintained is demonstrated conclusively when a large number of parasites is injected. Under such conditions phagocytosis is much more rapid and effective than in birds infected initially. In fact, it is well initiated within fifteen minutes after superinfection and within from 24 to 48 hours has so successfully operated that parasites can no longer be found in the peripheral blood. It is interesting to note that throughout our study the actual phagocytosis of the parasitized red cells is limited to the macrophages, that is, to the cells known under such various names as the hemophages of Kyes, the Kupffer cells in the liver, the pulp cells in the spleen, etc.

With this background it is possible to state very briefly our results on the cellular basis for immunity to superinfection. It will be recalled that when parasitized red cells were introduced into normal birds no appreciable phagocytosis of the organisms occurred before four hours and no distinct activation of the mesenchyme before 18 hours. In marked contrast to this when similar parasitized red cells were introduced into immune birds, phagocytosis was well initiated within 15 minutes and practically all of the parasites were removed within from 24 to 48 hours. The parasitocidal mechanism, then, involved in the destruction of the parasites at the time of the crisis, during the post-critical period, during latency and during immunity to superinfection, is primarily a cellular response of the host involving an activation of the mesenchyme. This activation, furthermore, is effective through two factors: (a) an actual increase in the number of phagocytic cells and (b) a greatly increased rate of phagocytosis by the individual macrophages.

The picture might be considered more or less complete were the activation of the mesenchyme non-specific, since then, of course, the absence of opsonizing antibodies would be accounted for, but Gingrich (1930)²⁹ has demonstrated that between *P. cathemerium* and *P. elongatum* the immunity is specific. Thus, during a latent infection with *P. cathemerium* there was an immunity to a superinfection of *P. cathemerium*, but not to an initial infection of *P. elongatum*, and *vice versa*. This demonstrates that the bird during latency acquires some mechanism which causes its phagocytes to ingest specific parasites and suggests either the production of a tropin

²⁸ P. R. Cannon and W. H. Taliaferro, *Jour. Prev. Med.*, 5: 37-64, 1931.

²⁹ W. Gingrich. Dissertation. Johns Hopkins School of Hygiene and Public Health, 1930.

which we have failed to demonstrate in our serological experiments, or a qualitative change in the macrophages. This whole question of the specificity of cellular responses in acquired immunity has been ably discussed in an earlier Harvey Lecture by Professor Gay (1931).²⁰

The question immediately arises: Does the picture which I have presented for avian malaria hold for malaria in man and other mammals? At the present time Mrs. Taliaferro and I are carrying out a similar study on *P. brasilianum* of Panamanian monkeys which is a quartan parasite almost identical with *P. malariae* of man. Similarly, Professor P. R. Cannon is making a study of the cellular reactions of the monkey to this infection. It is too soon to give you the final results of this work, but the following preliminary conclusions are justified. The entire picture of the ordinary course of the infection is similar to that in the bird with certain time differences. There is no indication of any inhibition of reproduction of the parasites, but the number curves show that plasmodicidal factors are operating. So far we have not been able to correlate the killing of the parasites with any plasmodicidal antibody, but only with the direct phagocytosis of the parasites by the differentiated macrophages. The cellular responses during the initial infection are similar to those in birds. There are increasing evidences of activation of the mesenchyme during the acute rise of the infection which reaches its height at the time of the crisis and slowly subsides as the developed infection progresses and latency is initiated. There is also a high degree of immunity to superinfection during latency, which can be demonstrated by the injection of washed parasitized cells into monkeys with a latent infection, but so far no work has been done on the cellular basis for this immunity.

In comparing the immune reactions in infections with *T. lewisi* and *P. cathemerium* it is quite remarkable that the immediate mechanisms of immunity and effects on the parasites are so different, and yet, that in both cases the immunity can be eventually ascribed to the macrophage system. Thus, in one case the immunity is associated with an antibody which inhibits reproduction and with one or more trypanocidal antibodies, whereas in the other case there is no inhibition of reproduction and the parasitocidal mechanism consists of direct phagocytosis without the intervention of any humoral tropin that has been demonstrated up to the present.

These investigations on the cellular phases of immunity to protozoan infections are but one phase of the growing mass of evidence indicating the rôle of the macrophages in general and local immunity, in antibody production, in chemotherapy and in normal

metabolism (see Linton, 1929;³⁰ Jungeblut, 1930, and Gay 1931).²⁰ There are many obvious similarities between the work which I have presented on these subjects. I would like particularly to mention the following: The cellular responses to malaria show a striking similarity to the morphological changes described by Epstein (1929)³² in the spleen and liver of the rabbit following the injection of such non-infectious antigens as sheep cells and horse serum. This is parallel very closely the conditions found in other infections, such as *Bartonella*, to cite a single example in which the cellular responses have been very accurately studied (see particularly Cannon and McClelland, 1929;¹⁹ Eliot and Ford, 1929,³³ and Morston-Gottesman and Perla, 1930¹⁶). And finally, although the cellular responses to malaria give rise to a general immunity, the same responses are probably elicited in so-called local immunity (see Gay, 1931¹⁸).

CONCLUSION

In concluding I wish to draw particular attention to the peculiar value of the blood protozoa for the study of what I believe to be some of the fundamental problems of immunity. All of these problems are related to the two great questions of how the host responds to infection and how the host's response affects the invading organisms. The advantages of the protozoa in studying these questions may be briefly summarized as follows:

(1) *The analysis of the effects of resistance on the invading organism.* The fact that some protozoa live in and are evenly distributed through the blood stream allows the study of the course of infection from day to day. The further fact that the protozoa are comparatively large permits the study of cell-division and their general behavior throughout the course of infection. Specifically, I have shown that taken together such studies differentiate sharply between those factors in the host's resistance which kill the parasite, i.e., parasitocidal factors, and those factors which inhibit cell-division, i.e., reproduction-inhibiting factors. Although parasitocidal factors, such as trypanolysins and direct phagocytosis of organisms are well known, we have been able to demonstrate in one infection a peculiar type of antibody-response which does not kill the organisms, but which inhibits cell-division. These methods of analysis probably can be applied to the smaller bacterial invaders although we have had some success in applying them to spirilla and chaetes.

(2) *The action of antibodies on the protozoa.* The

³⁰ R. W. Linton, *Arch. Path.*, 6: 488-501, 1929.

³¹ C. W. Jungeblut, *Ergeb. Hyg. Bakt. Immun. u. Exp. Therap.*, 11: 1-67, 1930.

³² E. Epstein, *Virchows Arch.*, 273: 89-115, 1929.

³³ C. P. Eliot and W. W. Ford, *Amer. Jour. Hyg.*, 10: 635-642, 1929.

same characteristics of the blood protozoa listed above permit the direct study of the action of antibodies on the invading protozoa *in vivo*. Thus, when an immune serum is tried curatively, it can be ascertained by direct blood examination whether the organisms are killed or not. Similarly, the action of the reproduction-inhibiting antibody can be observed, that is, the presence or absence of cell-division can be directly ascertained. Here again the only methods available for similar studies with the smaller bacterial invaders are at best indirect.

(3) *The cellular basis of immunity.* The blood protozoa have proved admirable material for the correlation of cellular responses with immunity, antibody formation, etc. Thus, in the study of the production of the reproduction-inhibiting antibody in *T. lewisi* infections, it has been possible to use the trypanosomes as a delicate measure of the activity of the macrophage system. Similarly, in the acquired immunity of birds to malaria it has been possible to correlate the course of infection and immunity with the cellular responses. In fact, the malarial organisms have proven to be particularly advantageous for this type of study not only because they are large and can be easily found in the tissues, but also because even after

digestion they leave a landmark for a considerable length of time in the form of the less readily digested pigment.

Lest I be misunderstood as suggesting the use of the blood protozoa for the study of all of the fundamental problems of immunology, I should also like to point out some of their shortcomings. Not even all the blood protozoa can be used for the studies I have presented this evening. Some of them, such as *T. cruzi*, the causative agent of Chagas's disease, form reproductive centers and localizations in the tissues which make the study of the normal course of infection by blood examinations impossible. Others, such as *P. falciparum*, the causative agent of estivo-autumnal malaria in man, although confined to the blood, show localizations in the capillaries of certain organs which thereby prevent the study of the course of normal infections by routine peripheral blood samples. The fact that the protozoa used in these studies are distributed throughout the blood stream prevents their use for studies in local immunity. Finally, inadequate cultural methods eliminate both the blood protozoa in particular and all protozoa in general as good material for the study of the serology and chemistry of immunological processes.

OBITUARY

ASHE, PIONEER FORESTER AND BOTANIST

THE death of William Willard Ashe on March 18, 1932, removes another distinguished name from the fast dwindling ranks of foresters who received their training in an era when the country was without established schools for education in the forestry profession. Ashe was born in Raleigh, N. C., on June 4, 1872, the oldest of nine children born to the Honorable Samuel A'Court Ashe and Hannah Emerson (Willard) Ashe. Ashe was noted as a boy for his love of nature, versatility, originality and for his mechanical and artistic ability. He was educated at the Raleigh Male Academy, the University of North Carolina (B. Litt., 1891), and Cornell University (M. S., 1892), specializing in geology and botany. He studied medicine for a while under Dr. W. I. Royster, of Raleigh. He was a member of the Sigma Alpha Epsilon fraternity. From 1892 to 1905 he served as forester of the North Carolina Geological Survey under Dr. J. A. Holmes. From 1905 until his death Ashe was an officer of the U. S. Forest Service, rising steadily in rank from forest expert and forest assistant to assistant district forester and senior forest inspector in "Region 7" (eastern United States). In 1906 he married a widow and distant cousin, Margaret Henry Wilcox. He had no children. Ashe was secretary of the National Forest Reservation Commission

and editor of its reports from 1918 to 1924. He was elected vice-president of the Society of American Foresters in 1919. He became a member of the Forest Service tree name committee in 1928 and was chairman from 1930 to his death.

Ashe was a true pioneer. He was one of the real fathers of the forest acquisition policy of the federal government and was among the first to recognize the need for forest research in this country. He planted one of the first commercial stands of long-leaf pine in North Carolina and discovered the secret of its successful transplantation. He is credited with introducing the modern cupping system in the American naval stores industry.

A bibliography of Ashe's scientific papers compiled by the writer covers 166 titles. He wrote extensively on systematic botany, logging costs, profitable forest management, land acquisition for conservation purposes, forest influences and forest types. One of the last papers he issued was a monograph of the genus *Polycodium*.

Ashe was an indefatigable observer, collector and annotator of plants. He published 510 new names in 35 genera. His taxonomic interests were (aside from his early papers in *Asarum* and *Panicum*) largely in connection with woody plants of the Southeast; 86 per cent. of his botanical novelties are in the five

families Rosaceae (including Malaceae), Ericaceae (including Vacciniaceae), Juglandaceae, Fagaceae and Poaceae.

Ashe was a quiet and retiring man, a hard worker, utilizing his personal time largely in study and writing; he was keenly observant, markedly original and independent, with a fine sense of humor, and with high standards of thought and conduct.

WILLIAM A. DAYTON

RECENT DEATHS

DR. WILLIAM W. KEEN, emeritus professor of surgery at Jefferson Medical College, Philadelphia, died on June 7 at the age of ninety-five years.

DR. NATHAN AUGUSTUS COBB, of the Bureau of Plant Industry of the Department of Agriculture, died on June 4 at the age of seventy-three years.

DR. VIRGIL COBLENTZ, of Philadelphia, formerly professor of chemistry in the New York College of Pharmacy and chief chemist of E. R. Squibb and Sons, died suddenly on June 10. He was seventy-six years old.

EDWIN JULIUS BARTLETT, professor emeritus of chemistry at Dartmouth College, died on June 10 at the age of eighty-one years.

HERBERT PARLIN JOHNSON, formerly assistant professor of zoology in the University of California and associate professor of bacteriology in the School of Medicine at St. Louis University, died suddenly on April 29 at the age of sixty-eight years.

THE death is announced on May 29 of Dr. Cuthbert

Christy, London naturalist, explorer and expert in tropical diseases. He was sixty-eight years old.

MISS NORA E. DALBEY, associate professor of botany, Kansas State College of Agriculture and Applied Sciences, who was carrying on special work in cytology while on leave of absence, died at Merritt Hospital, Oakland, California, on May 23. Miss Dalbey received her bachelor's and master's degrees from the University of Kansas. She has been at Kansas State College since 1918.

A CORRESPONDENT writes: "Anthony Spuler, associate entomologist of the Washington Agricultural Experiment Station, State College of Washington, Pullman, and Mrs. Spuler were drowned at Lake Wenatchee, Washington, on Memorial Day when their small motor boat capsized in a storm. Mr. Spuler received his bachelor's degree in zoology in 1917 and his master's degree in 1919 from the State College of Washington, and has been a member of the teaching and experiment station staff of that institution since his graduation. He was best known for his work in developing the use of moth traps as an indicator of the time to spray for codling moth control and for his research on oil sprays and other insecticides. Many of the results obtained in his investigations are the bases of established orchard practices in the Pacific Northwest."

Nature records the deaths of R. H. Adie, formerly secretary of the School of Agriculture, University of Cambridge, and the Hon. Mrs. Huia Onslow (Muriel Wheldale Onslow), university lecturer in plant biochemistry in the University of Cambridge.

SCIENTIFIC EVENTS

GIFTS TO THE BRITISH NATURAL HISTORY MUSEUM

AMONG the important acquisitions made by the Trustees of the British Museum (Natural History) and reported in the *London Times* are two considerable gifts from Mr. A. S. Vernay.

Some 60 mammals and 590 birds obtained by the Vernay-Lang expedition to the Kalahari Desert in 1930 have been presented by him, together with 264 flowering plants and ferns from the same region. The mammals include specimens of 11 forms described in South Africa as new to science, and the plant collections, from an area poor in flora and imperfectly known, make a welcome addition to the small representation hitherto possessed by the museum. The second gift from Mr. Vernay consists of 184 mammals, 29 reptiles, 34 fishes and 500 butterflies obtained by Captain Beresford Holloway, who accompanied the donor on his recent expedition to the Malay peninsula.

Other zoological gifts include 70 big-game trophies from India and Africa presented by Sir Richard Dane, and a collection made by Dr. E. B. Worthington during the Cambridge University expedition to the East African Lakes. In this are included 102 reptiles and amphibians, 900 fishes (including about 30 new species), and many molluscs and other invertebrates.

A gift to the Department of Botany is the British herbarium of the late Dr. John Thomas Irwin Boswell (1822-88), presented by Mr. F. J. Hanbury. This herbarium comprises about 20,000 sheets of well-mounted plants, contained in 14 mahogany cabinets. Boswell was the editor of the monumental third edition of the "English Botany," and was long connected with the Botanical Exchange Club as distributor. The accuracy and detail of his descriptions was based upon the material in this collection, which will be kept intact by the wish of the donor, who purchased it on Boswell's death. A collection of 372 Tanganyika

plants has been bought for the department of botany, and the department of geology has bought a specimen of the teeth of the extinct shark *Edestus* from the Devonian rocks of Rhenish Prussia.

Samples of volcanic dust which fell after the recent eruptions in the Andes have been presented to the department of minerals by the proprietors of *The Times* and by Messrs. H. W. Nelson, Limited. Professor G. Vibert Douglas has collected and presented a large series of rocks illustrating the geology and mineralization of several mines in the "copper belt" of Northern Rhodesia and Katanga, and purchase has been made of a series of exceptionally fine crystals from the Tsumeb copper mines in Southwest Africa. Copper, zinc and lead minerals are represented—among them cerussite, anglesite, chersylite, smithsonite and mimetite.

THE ENGINEERING SOCIETIES LIBRARY

THE Engineering Societies Library, New York, reports that, for the first time since the depression began, inquiries are falling off. Geographically, the decrease is uniform, indicating a lessening of industrial and engineering effort in all nations.

Library readers, however, continue to increase. They were ten per cent. more numerous in 1931 than in 1930, and they are still multiplying, according to Director Harrison W. Craver. The present economic situation, while slowing up the quest of industry for technical knowledge bearing upon problems of development, has stimulated the individual engineer to greater intellectual effort.

Jobless engineers and scientific men, according to Mr. Craver, are likely, in the long run, to profit by their enforced leisure, for, during the era of prosperity which came to an end in 1929, they were so immersed in the practical aspects of the tasks that they had little opportunity to keep abreast of engineering advances in other than their own specialized fields. Hence, it is believed, one result of the economic recession will be a broadening of the outlook of the professional engineer in all countries.

"Not until recently," Mr. Craver said, "did the depression affect us at all. Last year nearly 50,000 requests to supply technical information, a record number, were received. This represents a gain of several thousand over the previous year. But now, the slump in industrial operations is being reflected in a diminished demand for investigating service at the library.

Requests for facts, nevertheless, are coming from practically every country and from every state in the Union. They cover almost the entire range of engineering, according to Julian A. Sohon, chief bibliographer.

Soviet Russia, Mr. Sohon said, frequently asks for technical advice through the office of the Amtorg in New York. American engineers working in Russia also write for assistance from time to time.

The New Zealand Government is another conspicuous source of queries, particularly with respect to public works. Many Swedish engineers also turn to the library, which, despite the low ebb of engineering activity, is developing its facilities in preparation for a great industrial era which, engineers believe, lies ahead.

The library is the largest strictly engineering library in America, and probably in the world. It now contains 128,000 volumes, 5,000 pamphlets, 6,321 maps and 3,872 searches. Allen S. Miller, of New York, is chairman of the Library Board for 1932.

FIELD CONFERENCE OF PENNSYLVANIA GEOLOGISTS

THE second annual field conference of Pennsylvania geologists was held in the Lehigh Valley on May 28, 29 and 30, the geology departments of Lehigh University and Lafayette College acting as hosts. Especial mention should be made of the efficient manner in which the trips were planned and carried out, thanks to the able work of the committee in charge, consisting of D. Fraser, A. H. Fretz, B. L. Miller and L. Whitecomb, of Lehigh, and C. K. Cabeen, H. A. Itter, H. Koerner and F. Ward, of Lafayette. About 75 members and guests from outside Pennsylvania registered at Markle Hall, Lafayette College.

On the afternoon of Saturday, May 28, two field trips were offered simultaneously, the visitors choosing between them. Trip No. 1, under Professor Itter, of Lafayette, covered the three members of the Triassic System exposed along the Delaware below Easton, the well-known "Ringing Rocks" and certain exposures of the Cambrian and Pre-Cambrian. Trip No. 2 visited the cement and slate belts of the Lehigh Valley, including quarries and mills, and proved of unusual interest to the non-metallic economic geologists. It was in charge of Dr. B. L. Miller, of Lehigh University. The Saturday activities finished with an informal dinner at Easton. President W. R. Lewis extended a welcome from Lafayette College, and various members spoke very briefly upon the local geology. During a short business session the by-laws drawn up by committee were adopted. These included the appointment of a permanent secretary-treasurer, who must be a member of the Pennsylvania State Geological Survey. Dr. Bradford Willard was selected for this position.

The Sunday, May 29, trip was attended by the entire assembly. The party left Easton by automobile

and proceeded up the Delaware Valley to the Water Gap, thence to Stroudsburg, crossed to the Lehigh River, and thence traveled south to Bethlehem. The trip included visits to exposures of most of the formations from the Pre-Cambrian through the Upper Devonian beside Pleistocene deposits and various economic features such as cement, slate and metallic paint ore. The excursion was successively led by Professor Freeman Ward, of Lafayette, Dr. Bradford Willard, of the State Survey, Professor Frank Swartz, of Pennsylvania State College, and Dr. B. L. Miller, of Lehigh University. At Bethlehem dinner was served at the Hotel Bethlehem and was followed by a welcome from President C. R. Richards, of Lehigh, after which Professor H. Ries, of Cornell, spoke briefly.

On the thirtieth the conference ended in the members and guests selecting one of three trips. The first under Dr. B. L. Miller, of Lehigh, was largely devoted to metallic economic geology in that visits were made to abandoned iron pits and the old zinc mines of the Saucon Valley south of Bethlehem. The second trip, conducted by Professor Freeman Ward, of Lafayette, was devoted to a study of the glacial deposits, chiefly with a view of observing the differences between and the interrelations of the Illinoian and Wisconsin drifts. Those who selected the third trip were led by Dr. Lawrence Whitecomb, of Lehigh, to Spitzenberg, a conical hill near Lenhartsville, some thirty miles west of Bethlehem. The purpose of this visit was to inspect the peculiar limestone conglomerate which rests upon the Ordovician shale near the crest of the hill.

It is planned to hold the annual meeting of the conference for 1933 at Harrisburg as guests of the Pennsylvania Topographic and Geologic Survey. This is scheduled tentatively for the last week-end in May and will cover the Silurian-Devonian-Mississippian sections of the Susquehanna and Juniata Valleys, the Triassic and pre-Silurian Paleozoics between Harrisburg and York, including a visit to the Cornwall Iron Mines, and the river terraces, the peneplanes, and other physiographic features of the neighborhood.

BRADFORD WILLARD,
Secretary-Treasurer

THE NEANDERTAL RACE IN PALESTINE

THE discovery during the first two weeks in May of seven skeletons of the Neandertal race is destined to throw a flood of light on that particular species of fossil man. The specimens hitherto found in Europe have been so few and fragmentary that there was little evidence to suggest that the race or species might include a number of varieties. The first intimation of marked variation came with the discovery of the skull at Broken Hill, Rhodesia, some ten years ago. In 1925 Turville-Petre found a portion of the cranial cap of a Neandertal skull in the Cave of the Robbers near the Sea of Galilee. But the fragment being small (frontal and one cheek bone) gave no indication of variation from the European type.

The seven individuals just found in the Cave of the Kids near Haifa by Theodore D. McCown, field representative of the American School of Prehistoric Research and in charge of the joint excavations of the American and British Schools, will, on account of their relative completeness, throw new light not only on the species as a whole, but also point to a Palestinian variety of the Neandertal species. A tracing just received of one of the best preserved adult skulls shows that the latter agrees with the European type in the marks of a powerful musculature, massive brow ridges, taurodont dentition and prognathism. But the prognathism is confined largely to the upper jaw and the dentition. The chin can scarcely be called receding and the frontal and parietal portions of the skull are more highly developed than in the known European examples.

It is especially fortunate that these seven skeletons, as well as that of a Neandertal child found (also by McCown) in the same cave one year ago, were all *in situ* and associated with industrial remains of the Mousterian Epoch. McCown states that one of the adult skeletons was found clasping to his breast a huge jaw of the wild boar.

The skeletons were lying near the bedrock and in a stony matrix. McCown is bending every effort to remove them safely from the deposit and ship them to London in time for exhibition at the International Congress of Prehistoric and Protohistoric Sciences which meets from August 1 to 6.

GEORGE GRANT MACCUDY

SCIENTIFIC NOTES AND NEWS

THE preliminary program of the meeting of the American Association for the Advancement of Science, to be held at Syracuse, New York, from June 20 to 25, was published in the issue of *SCIENCE* for May 27. Some seventeen associated scientific societies will meet with the association. The first general session, fol-

lowed by a reception, will be held on the evening of Monday, June 20, under the presidency of Dr. John J. Abel, professor of pharmacology, emeritus, at the Johns Hopkins University. Dr. Edward L. Thorndike, professor of educational psychology at Teachers College, Columbia University, will make the address.

The first meeting of the council will be held at 9 o'clock on Tuesday morning. As has been noted in the preliminary announcement, there will be a full program of symposia and general addresses with special opportunities for excursions and field trips.

NEW YORK UNIVERSITY conferred at its graduation exercises the doctorate of science on Dr. William H. Welch, professor emeritus of the history of medicine at the Johns Hopkins University, who was from 1879 to 1884 professor of pathological anatomy and general pathology in the New York University and Bellevue Hospital Medical College.

THE University of Würzburg, at the three hundred and fiftieth anniversary of its foundation on May 2, conferred the degree of doctor of medicine *honoris causa* on Dr. Francis G. Benedict, director of the Nutrition Laboratory of the Carnegie Institution of Washington.

THE honorary degree of doctor of science was conferred on June 16 by George Washington University on Dr. Frederick Parker Gay, head of the department of bacteriology in the College of Physicians and Surgeons of Columbia University; on Dr. George Canby Robinson, director of the New York Hospital and Cornell Medical Association, and on Dr. Alan Mason Chesney, dean of the Johns Hopkins University School of Medicine.

THE degree of doctor of science will be conferred on Dr. Walter C. Mendenhall, director of the U. S. Geological Survey, by the University of Wisconsin, on June 20.

AT the seventy-seventh annual commencement of the Polytechnic Institute of Brooklyn the honorary doctorate in science was conferred upon Dr. Moses Gomberg, chairman of the department of chemistry at the University of Michigan, and on Professor Irving Wetherbee Fay, of the institute, who becomes professor emeritus of chemistry after thirty-five years of service at the college.

THE staffs of the College of Engineering and the Engineering Experiment Station of the University of Illinois gave a dinner on May 25 in celebration of a decade of progress of the College of Engineering under the guidance of Dr. Milo S. Ketchum as dean of the College of Engineering and director of the Engineering Experiment Station. Short addresses were made by Dr. A. N. Talbot, Assistant Dean H. H. Jordan and Professor W. C. Huntington. Professor A. C. Willard presented an illuminated parchment to Dean Ketchum on behalf of the members of the staffs of the College of Engineering and the Engineering Experiment Station. Dean Ketchum made a brief response. The parchment contained the following

note of appreciation: "The staffs of the College of Engineering and the Engineering Experiment Station of the University of Illinois upon the completion of a decade of service by Milo Smith Ketchum as dean and director unite in expressing to him their appreciation of his able guidance and leadership in the affairs of the college and station during the ten years and in wishing him every success in the years that are to come."

THE Society for Experimental Biology and Medicine at its recent annual meeting elected the following officers: *President*, A. R. Dochez; *Vice-president*, E. L. Opie; *Secretary-Treasurer*, A. J. Goldforb; *Council*, W. B. Cannon, A. E. Cohn, L. J. Cole, W. O. Fenn, M. S. Fleisher, W. H. Harris, W. J. MacNeal, W. Ophüls, W. J. V. Osterhout, W. W. Palmer, S. W. Ranson, F. R. Sabin, F. H. Scott, R. W. Scott, C. M. Van Allen and E. Witschi.

DR. GEORGE W. BACHMAN has been appointed director of the School of Tropical Medicine, San Juan, Puerto Rico. The school is under the auspices of Columbia University. Dr. Bachman, who has been acting director of the school for the last year, succeeds Dr. Earl B. McKinley, who resigned to become dean of the George Washington University School of Medicine. Dr. Bachman was also promoted from associate professor to be full professor of parasitology.

DR. JAMES W. GLOVER, who has been on leave of absence from the University of Michigan, and who has been president of the Teachers Insurance and Annuity Association of America, has resigned from his position in the association and will resume his professorship of mathematics at the University of Michigan beginning with the coming academic year.

PROFESSOR R. S. SETON, head of the department of agriculture of the University of Leeds, retires at the end of the academic year.

THE Committee on Scientific Research of the American Medical Association has given to Dr. Daniel A. McGinty, of the department of physiology, Emory University Medical School, a grant for the continuation of studies on the coronary circulation. Two previous grants for similar work have been given to Dr. McGinty by the committee.

THE Barnard Free Skin and Cancer Hospital, St. Louis, has been awarded a grant by the American Medical Association, for a study of the problem "The Potential Infiltrative Nature of the Virus of Warts" to be carried out under the direction of Dr. M. G. Seelig.

CURATOR FRANK C. BAKER, of the Museum of Natural History, University of Illinois, will continue his studies of the pulmonate fauna of the state of Illinois,

begun last summer, for the State Natural History Survey of Illinois. He will be assisted by Mr. Dale Foster, graduate student in zoology of the university. Particular attention will be given to the valley of the Mississippi River, which will be surveyed from Jo Davies County to southern Illinois.

MR. SEIDO ENDO, instructor in geology at Tohoku Imperial University, Sendai, Japan, is spending the next two years in paleobotanical studies with Professor E. W. Berry at the Johns Hopkins University.

DR. W. MCKIM MARRIOTT, dean and professor of pediatrics, Washington University School of Medicine, St. Louis, will be the lecturer at the University of California Medical School for the year 1932-1933. Dr. Marriott, who will be at the medical school early in the fall of this year, will conduct lectures and clinics.

DR. RUDOLPH MATAS, emeritus professor of surgery, Tulane University of Louisiana School of Medicine, New Orleans, delivered the sixth annual Donald C. Balfour Lecture at the University of Toronto Faculty of Medicine, on "The Story of Postoperative Pulmonary Embolism before and after Lister." The date was the one hundred and fifth anniversary of the birth of Lord Lister.

THE Herbert Spencer lecturer for this year was Dr. Ronald Aylmer Fisher. The lecture was given on June 8 under the title of "The Social Selection of Human Fertility."

PROFESSOR C. U. ARIËNS KAPPERS delivered the David Ferrier Lecture at the Royal Society on June 2, taking as his subject "Some Correlations between the Brain and the Skull."

PROFESSOR WERNER HEISENBERG, of Leipzig, Professor George Gamow, of Leningrad, and Professors Samuel A. Goudsmit and David M. Dennison, of the University of Michigan, will participate in the fifth Symposium on Theoretical Physics to be given at the University of Michigan during the summer session, June 27 to August 19. The lectures by Professors Gamow, Goudsmit and Dennison will begin on the opening day of the session, June 27. Due to the fact that Professor Heisenberg will be detained in Leipzig on account of official duties at the university his lectures will not begin until Monday, July 11.

THE thirty-fifth annual meeting of the American Society for Testing Materials will be held in Atlantic City from June 20 to 24. On Tuesday, June 21, symposia will be held on "Textile Materials" and on "Steel Castings." On Wednesday sessions will be devoted to steel, magnetics and insulating materials. The seventh Edgar Marburg Lecture, "Fundamentals in the Prob-

lem of Resistance to Deterioration," will be given on Wednesday afternoon by Professor Hugh S. Taylor, of Princeton University. Sessions will be held on Thursday for discussion of the effects of temperature on metals, timber, coal, paving and waterproofing materials and corrosion and fatigue of metals. On Friday programs will be held devoted to cement, lime, gypsum, ceramics, non-ferrous metals, concrete and building stones.

SIGMA PI SIGMA, the honorary physics fraternity, installed its twenty-fourth chapter at Miami University, Oxford, Ohio, on June 4. The chapter is designated the Omega chapter. The charter group was composed of about twenty undergraduates, graduate students and faculty members, including Dr. R. L. Edwards, head of the department of physics. Dr. Marsh W. White, of the department of physics at the Pennsylvania State College and executive secretary of the fraternity, was the installing officer. At an open meeting of the chapter following the installation dinner Dr. White gave an address on "Nuclear Physics."

THE section of geology of the Ohio Academy of Science held its annual spring field excursion on May 28 and 29, in southern Ohio, devoting attention exclusively to the physiography of the region, especially the drainage changes since preglacial time. The Teays Valley and its tributaries were examined in the area between Portsmouth and Athens, and the relations between the Teays, Deep and present stages were observed. Twenty members, guided by Wilber Stont, state geologist of Ohio, constituted the party.

THE one hundredth anniversary of the founding of the British Medical Association will be celebrated at the annual session in London from July 21 to 30. The annual representative meeting will be held on July 21 and the three following week days, while the scientific sections will meet on July 27, 28 and 29. The annual general meeting will be held on July 23, at the British Medical Association House in London.

IN opening the new reading rooms at the Institute of Physics, London, on May 24, Lord Rutherford, the president, explained that they were provided to give greater opportunities to the members of the institute and its participating societies. Through the cooperation of the Physical and Optical Societies and the other participating societies, a large number of books and periodicals had been provided. The intention was to gather together a small library of text-books and reference books, and the nucleus of such a library already existed. At the annual general meeting held afterwards, Lord Rutherford said that remarkable progress had been made in the short time

since the foundation of the institute. He considered that the institute could justly claim some of the credit for the growing recognition of the value of applied physics, and he urged physicists of every type to regard it as a duty to join the institute. Lord Rutherford was reelected president, Sir Frank Dyson and Sir William Bragg were elected honorary fellows.

WILLIAM H. DONNER, of Villanova, retired steel manufacturer of Pittsburgh, has been elected president of the newly established International Cancer Research Foundation. Mr. Donner, it is understood, has placed at the disposal of the foundation cash and securities on the basis of present values amounting to \$2,000,000. This was set aside by Mr. Donner as a trust in 1929 on the death of his son, Joseph W. Donner. Arthur Morton, president of the Pennsylvania Hospital, Philadelphia, is the vice-president of the foundation. The directors are: Thomas S. Gates, president of the University of Pennsylvania; Edward R. Weidlein, of the Mellon Institute for Industrial Research, Pittsburgh, and former United States Senator George Wharton Pepper. In addition to the directors who will administer the foundation, there will be a board of advisory trustees to be selected from among distinguished citizens and scientific men in all parts of the world. They will advise on the selection of the most promising research problems and investigators and decide where the foundation's money can be expended most efficiently. The foundation, it was stated, is interested primarily in securing results by assisting qualified investigators, and money will not be spent on buildings. The foundation stipulates that not more than 35 per cent. of its income shall be allotted to one institution, not more than 50 to 65 per cent. within the United States, and not less than 35 nor more than 50 per cent. outside the United States.

ONE of Audubon's three largest and finest canvases, an oil painting of "Black Cocks" on a grouse moor, has been presented to the Harvard Museum by John Eliot Thayer. Mr. Thayer has recently given the museum his collection of birds' eggs and nests. The painting was done by Audubon in 1827 while he was on a visit to Scotland. It was painted for a Scottish nobleman whose family sold it some years ago to Mr. Thayer. The canvas is about six by nine feet and has the qualities of an eighteenth century landscape.

THE Carnegie Corporation has made an appropriation of \$10,000 toward the maintenance of the library of the Medical College of Virginia, which will this summer be housed in a new building. Adjoining the new library of the college the Richmond Academy of Medicine has built its home and library. This will contain the Joseph L. Miller collection of rare first

editions, engravings, silhouettes, medical curios, etc. The headquarters of the Medical Society of Virginia will also be in the Academy of Medicine building.

AN offer to pay at the rate of £5,000 a year from July 31, 1932, to July 31, 1933, for the maintenance of an Imperial Forestry Institute in Oxford has been made by the Forestry Commission and the Secretary of State for the Colonies. The only condition is that the university shall make a contribution to the Department of Forestry for the same period at a rate not exceeding £288 a year, in addition to the contribution which was current on March 18, 1924.

THE annual report of the Royal Society for the Protection of Birds, according to the *London Times*, refers to the need for protection for insectivorous migratory birds, in their nesting homes, in lands where they winter, and on passage. The report says that the dramatic rescue of migrating swallows and martins by Austrian and Hungarian animal-protection societies during the sudden snows in the autumn of 1931, and their transportation by aeroplane to warmer lands, threw for a few weeks a floodlight on the subject of migration, and should suggest a sequel more practical than an ephemeral story and photograph. It should spur on investigation into the value of migratory birds and stimulate rational protection. Reported greetings accorded the swallows in Venice contrast oddly, however, with familiar accounts of migrants netted by the *roccoli* and dished up at restaurants, swallows taken at their roosts for millinery, martins' nests knocked down to inculcate tidiness in paper-littered streets. It is stated that the most notable protection afforded migrating birds at present lies in the bird-nests and perches at six lighthouses on migration routes, provided by the society in cooperation with Trinity House. With regard to oil pollution, it is urged that international action can alone remedy an evil for which ships of all nations are responsible.

The *Geographical Journal*, London, has received through the agency of the High Commissioner for Canada the final figures of population by provinces arrived at through the census taken on 31 May-1 June 1931 by the Dominion Bureau of Statistics. A comparison with the figures for 1921 shows that the total population is 10,374,196, an increase of over 1,500,000 over 1921; and all the provinces, except four, show percentage increases varying from 5 to 30 per cent. The very small population of Yukon Territory has grown by seventy-three persons, but Prince Edward Island, Nova Scotia and the North-West Territories all register a decrease, in the last case of more than 10 per cent. Quebec has the largest numerical increase (513,056), closely followed by On-

tario with 498,021; a drop of about 11,000 is recorded by Nova Scotia.

THE Alliance nationale pour l'accroissement de la population française, in a study it has recently published on the vital statistics of France for 1931, points out, according to the Paris correspondent of the *Journal* of the American Medical Association, that the birth rate fell off sharply toward the close of the year. A comparison of the birth rate for the corresponding quarters of 1930 and 1931 shows the following differences: first quarter, increase 937; second quarter, decrease 3,537; third quarter, decrease 4,907; fourth quarter, decrease 11,155; for the entire year, decrease 18,662. The number of marriages, furthermore, having diminished by more than 16,000 it is to be feared that the reduction in the number of births may be still greater in 1932. If one notes that, of the 730,000 births in 1931, 55,000 were of children of foreigners, whereas, of the 680,000 deaths, there were only 30,000 deaths of foreigners, it will be seen that the French excess of births over deaths in 1931 was only 25,000. This small excess runs the risk of being transformed next year into a permanent deficit unless something energetic is done to promote a better birth

rate. Finally, since the number of emigrants in 1931 exceeded the number of immigrants by more than 25,000, the population of France has in reality diminished, the first time that that has happened since the war.

A 6,000-ACRE experimental forest, to be used as a "laboratory" for forestry experiments and research, has been established in the Lassen National Forest in California. The tract contains over 3,000 acres of red and white fir timberland on which both mature and small trees are available for future experiments in forestry methods of timber cutting, logging and slash disposal. One fifth of the area is covered with brush fields, the result of repeated fires. Here reforestation will be undertaken by the planting of stock grown at the Forest Service nursery at Susanville, in order to convert those brush fields into commercial forest. Later, one or more portions of the experimental forest will be selected and designated as "natural forests" and will be left unmolested for the purposes of scientific study. The Swayne Mountain Experimental Forest, the first to be established in California, will be under the supervision of the California Experiment Station of the Forest.

DISCUSSION

PHYSIOGRAPHY AND THE DYNAMIC CYCLE

INTRODUCTION

IN an article in *SCIENCE* and in other recent papers Waldo S. Glock¹ has presented theoretical discussions of several aspects of the physiography of the lands. Contributions to the theory of a relatively new subject are especially welcome, for whether or not they lead to definitive conclusions they incite students to more careful reflection on fundamental principles of their science.

Glock suggests the division of physiography into two phases, an active or dynamic phase which he would call geodynamics, and a static or passive phase, called geomorphology. "Physiography may be approached from a purely dynamic view-point." Accordingly he discusses a "dynamic cycle" supposed to be measurably independent of and in any case different from the "geographic cycle."

The "dynamic cycle of stream systems" is contrasted with the "geographic cycle" of landforms. "A stream is never young, never mature, and never old in a strictly dynamic sense, for the processes, although

they vary in intensity, vary little if at all in quality." In the dynamic cycle streams first pass through a phase of extension, "a time of conquest and minute invasion"; later through a phase of integration, "a time of withdrawal and consolidation," in which tributaries are eliminated "until merely a skeletonized framework remains to care for drainage." These two phases are not necessarily distinct but may overlap, at least locally.

Geomorphology is regarded as static or passive, and "is concerned with the details of surface configuration expressed first by the origin of that form and second by the influence of lithology and rock structure. The method of origin has interest only because it explains and rationalizes important lineaments in the composition of the landscape." The geographic cycle "stands out as the quintessence of geomorphological description."

WHAT IS PHYSIOGRAPHY?

In 1869 Huxley delivered a series of twelve lectures on natural phenomena under the auspices of the London Institution. To distinguish his subject from the elementary works on physical geography of his day he borrowed the term "physiography" which had long been applied, in a different sense, to a department of mineralogy. The lectures were published in 1878 under the title "Physiography, an Introduction to the

¹ Waldo S. Glock, "Dual Nature of Physiography," *SCIENCE*, n. s. 72, pp. 3-5, 1930; "The Development of Drainage Systems and the Dynamic Cycle," *Ohio Jour. Sci.* 31, pp. 309-334, 1931; "The Development of Drainage Systems: A Synoptic View," *The Geogr. Rev.*, 21, pp. 475-482, 1931.

Study of Nature." While no attempt was made to present a complete or balanced treatise, we find chapters on the figure of the earth, its movements, and the sun; on the atmosphere, rain and dew, snow and ice, and evaporation; on the sea and its work, coral land, and the distribution of land and water; and on the land and land waters, earthquakes and volcanoes. Huxley did not present his chapters in the order given above, nor name the groupings of chapters actually employed; but it is clear that for him "physiography" in its newly adopted usage comprised the earth as a globe in the solar system, the atmosphere, the oceans and the lands.

In the latter part of the nineteenth century the term "physiography" began widely to be substituted for physical geography, particularly for the more advanced study of physical geography, including everything commonly comprised by the double term. The literature of this period contains frequent repetitions of the expression "physical geography, or physiography," thus showing how fully the two terms were regarded as identical. As Davis² wrote in 1902, "In recent years there has been a tendency to compress the name (physical geography) into the single word 'physiography'"; and the content of the subject he thus sets forth: "The four chief divisions of physiography are the earth as a globe, the atmosphere, the oceans, and the lands."

This conception of the term "physiography" has endured to the present time, and of six general textbooks on physiography before me, all but one treat the four standard subdivisions of the subject as enumerated above by Davis. The one exception treats three out of the four subdivisions. It is true that certain regional physiographies deal only with physiography of the lands or of the lands and the atmosphere (especially climate). It is equally true that in America, where instruction in physiography has commonly been given in departments of geology and where the physiography of the lands has been emphasized as of particular interest to geological students, some geologists have come to think of physiography as relating only to the lands. But these exceptions should not blind us to the fact that "physiography" has enjoyed wide-spread and long-established usage as a convenient term by which to denote the serious scientific study of man's physical environment in its fourfold character. Our dictionaries and encyclopedias recognize this usage as the standard one, and it is exceptional when one records the fact that the term is "limited by some to that branch of the subject dealing with the land."

² W. M. Davis, "The Progress of Geography in the Schools," First Year Book National Society for the Scientific Study of Education, Part II, pp. 7-49, 1902.

The four subdivisions of physiography have grown to dimensions justifying special names. The earth as a globe is perhaps more often treated under the not wholly satisfactory terms "astronomical geography" or "mathematical geography," than under more technical but possibly more satisfactory names. Physiography of the atmosphere has become the modern meteorology and climatology. Physiography of the oceans is often called oceanography, or physical oceanography, to distinguish it from biologic aspects of the sea. For physiography of the lands the term geomorphology has gained wide usage here and abroad.

It is with these general considerations in mind that the reader should weigh Glock's suggestions regarding physiographic terminology and methods of physiographic study. Apparently Glock would restrict the term "physiography" to physiography of the lands. Even when he employs the older term "physical geography" he tells us that "physical geography has a dual nature," and divides it into two parts only just as he does physiography, with both its "active" and "passive" phases relating to land surfaces. The readers must therefore consider first whether it is wise to restrict the term physiography to a single field, the lands. If so, what name should one give to the unified advanced study of man's fourfold physical environment, now commonly called physiography?

DYNAMIC GEOLOGY AND PHYSIOGRAPHY

As Glock points out, it is possible to study processes from the purely dynamic point of view, without taking account of the resulting land forms. Such studies have long been prosecuted, and have usually been considered a part of dynamic geology. Undoubtedly much more remains to be accomplished in this field. The only questions to be considered are whether it is wise to classify these studies in dynamic geology as a branch of physiography of the lands; and, if so, as to whether this branch should be called "geodynamics" instead of "dynamic geology." If the writer correctly understands Glock, there are no topics which would ordinarily be included in his geodynamics (where forms are not to be considered and where processes are to be viewed from the dynamic standpoint alone) which would not fall naturally and necessarily into the field of dynamic geology. Nor does geodynamics seem a less inclusive term than dynamic geology. If the two terms are essentially synonymous, this particular question is reduced to a choice between an older and a proposed newer usage.

On the more fundamental question as to whether purely dynamic geological studies should be classed as physiography, opinions may differ. Certainly some texts on physiography have so far emphasized

the study of forces as to leave only secondary and partial emphasis on the study of the resulting forms. Not a few physiographers have voiced the criticism that such works are really treatises on dynamic geology rather than on physiography. Such criticism reflects the prevailing tendency to consider studies of processes from the purely dynamic point of view as lying outside the field of physiography, and to call such studies by the time-honored name "dynamic geology."

PHYSIOGRAPHY OF THE LANDS AND GEOMORPHOLOGY

For most workers in the subject, "physiography of the lands" and "geomorphology" are synonymous terms. Neither term implies the study of processes of and for themselves, any more than either implies the study of geologic structures of and for themselves. Such studies are left to workers in the classic fields of dynamic geology and structural geology. The physiographer (of the lands), or geomorphologist, does of course concern himself much with processes and structures, just as does the economic geologist, the stratigrapher and workers in other branches of geologic science. But he deals with both merely as factors in the evolution of land forms, which latter is the real object of his study. He touches lightly or leaves untouched many aspects of dynamic geology which are vitally important from the dynamic point of view, but which throw relatively little light on the evolution of the earth's surface features. So also in structural geology he is forced to pass by many fascinating questions which concern him less directly than other aspects of that field.

In short, the geomorphologist recognizes the existence and the importance of two vast fields, dynamic geology and structural geology, each well worth cultivating for itself alone, but each quite distinct in objectives, methods and in much of its subject matter, from his own field—physiography of the lands. From those neighboring fields he draws what he needs for the understanding of his special problems, just as he expects the dynamic geologist and the structural geologist to take from geomorphology everything which will help to elucidate their problems. But he does not forget that there is a real independence as well as an interdependence of the three fields of investigation.

THE NATURE OF GEOMORPHOLOGY

The content of geomorphology is reasonably well established, both by definition on the part of experts in the subject and by common usage of workers in the field. It comprises the study of the origin and evolution of the surface features of the earth in terms of "structure, process and stage." Of the three terms

of this trinity, elaborated by Davis in many of his writings, *structure* is the only static or passive element. The *process* is the active vitalizing factor without which there could be no cycle of land-form evolution; and the *stage* of the cycle is a transitory phase of the ever-changing record of the extent to which the active process has operated.

In a day when the only scientific geography was physical geography or physiography, it was perhaps natural that the cycle of land-form evolution should be called "the geographic cycle." To-day "geographic" has a very different connotation. Modern geographers may not agree as to the scope of their subject; but a large proportion of them define its essence, in one form or another, in terms of the relation of organic life to physical environment. The geographer thus puts emphasis not only upon life and its relations, but also upon physical environment as it is to-day. For him the physical environment may perhaps be said to represent the static or passive phase of his study. The cycle of land-form development is not "geographic" in this modern sense of the term. It is "geomorphic," however, and can perhaps best be called the *geomorphic cycle*.

Since the geomorphologist is dealing, in terms of structure, process and stage, with ever-changing cycles of land-form evolution, his point of view can never be static or passive. He studies the effects of geologic processes operating upon geologic structures throughout significant periods of geologic time. Only thus can he understand and interpret the evolution of the earth's surface features. Whether or not the dynamic geologist can afford to ignore surface form in his dynamic studies, it would seem that the geomorphologist must always think in terms of progressive changes effected by dynamic action.

DOUGLAS JOHNSON

COLUMBIA UNIVERSITY

AN APPEAL TO ANTHROPOLOGISTS

AVAILABLE information on the color of the iris at birth is meager and inaccurate. The popular generalization that "all white infants have blue eyes" is still widely quoted, although any obstetrician, midwife or nurse who has noticed the irises of many new-born infants can recall that some are totally brown, some are blue-green and some are mixed brown and blue or blue-green. It is well known also that during infancy significant changes in iris coloration occur, especially in those which are initially some type of blue. No positive information seems to be available as to whether the initially brown irises desaturate, and whether in the extremes of such cases they become finally some type of blue with or without partial brown patterns (in streaks, flecks or rings surround-

ing the pupil). Just how rapidly the major changes in coloration occur is unknown, although general opinion is to the effect that the "final" color is attained some time between the first month and the first year of post-natal life. However, general observation again suggests that throughout life marked changes occur. It is obvious that each of these factors must be considered in any adequate evaluation of the ethnological significance of iris color, as well as in any detailed study on the inheritance of this characteristic.

Through the cooperation of the department of obstetrics of the Johns Hopkins University, conditions favorable to the type of study just outlined have been placed at our disposal. Observations made so far present many new points of interest, which diverge from the commonly accepted opinions noted above. Moreover, problems have appeared which will call for a major series of investigations involving the cooperation of embryologists, oculists, chemists, physicists and others. By the end of the summer we hope to have a preliminary report ready, setting forth the import and complexity of the problem with the methods developed, and results of preliminary observations. In the meantime, we wish to invite the cooperation of anthropologists who are stationed in, or who plan expeditions to various parts of the world, in obtaining data on the iris coloration at birth, and on changes during the first year, for various stocks; especially those not available in the Eastern United States. Of special importance will be data on stocks which have been hybridized very little during recent times.

One of our ultimate goals will be the development of a scale which is both reproducible and graduated in more adequate steps of hue, saturation and pattern than any existing scale; and we are using methods by which our color standards can be specified in physical units; nevertheless, for present purposes, reports made in verbal terms will yield useful information. Descriptive terms such as those listed below, together with approximate descriptions of patterns due to intermixtures of color, are sufficiently differentiating to indicate variations of major importance. Such data are admitted to be unreliable, but where so little is known, rough data are indispensable to the planning of accurate measurements.

The following color terms include many of the differentiations of eyes at birth as so far observed, and are suggested as constituting the basis of a scheme which may give some uniformity of report for different observers. Of course, qualifying words may be needed in certain cases, and when the eye color falls outside of this list appropriate additional terms will need to be used.

Light yellowish brown	Light greenish blue
Dark yellowish brown	Dark greenish blue
Light reddish brown	
Dark reddish brown	Dark purple
Very dark brown	Lavender
Light blue	Pale red
Medium blue	Ruby red
Dark blue	Orange red
Very dark blue	
Gray blue	

Special points to be noted are indicated by the following questions:

(1) Is the iris of approximately a single color evenly diffused?

(2) If the iris is a mosaic of two or more colors, what is the relative distribution and general character of the pattern; *e.g.*, does one color form a ring at the edge of the iris, or an irregular patch, or does it occur in flecks or streaks? What relative proportions of the iris are occupied by the various colors? An approximate description of the pattern would be desirable.

(3) At birth is the iris cleared, or is there a hazy coat of slaty blue or other color uniformly distributed; or is part of the iris thus covered, part of it being cleared and having another color? How early does the hazy coat disappear and the iris become cleared, and what is its color at this time?

(4) During the first few months do eyes which initially are totally blue change to brown, and do in some cases eyes which initially are brown change to totally blue or a smaller area of brown?

(5) What is the color of the sclerotic coat of the eye; is it "white" or is it bluish, brownish, etc.?

KNIGHT DUNLAP
W. C. BEASLEY

THE JOHNS HOPKINS UNIVERSITY

A FURTHER NOTE ON THE ANALYSIS OF ELECTROMYOGRAMS

IN a recent issue of SCIENCE, Davis, Forbes and Garceau¹ commented upon a method described by Travis and Hunter² for studying voltage-frequency relationships in action currents. Travis and Hunter may be criticized for not making clear certain points relative to the applicability of their method, but the method itself does not appear to deserve the criticism offered against it by Davis, Forbes and Garceau.

In the main Travis and Hunter's method is one for the treatment rather than for the elucidation of the origin and ultimate nature of action current potentials. It was designed to give an effective value

¹ H. Davis, A. Forbes and L. Garceau, SCIENCE, April 22, 1932.

² L. E. Travis and T. A. Hunter, SCIENCE, February 19, 1932.

for either regularly or irregularly appearing action current waves. However, it does not assume that the waves originally produced were made up of the frequencies revealed by the electrical analysis. The method appears to be an improvement over the practice of merely presenting and describing actual pictures of action currents. No physicist would venture to compare or describe waves from their pictures alone. He knows well that two waves may be quite similar pictorially but turn out to be very dissimilar when analyzed.

Although the method is certainly applicable to the study of repeating waves and much of value may be expected from such a study, it is the only means at our command now to evaluate quantitatively non-repeating waves. Inasmuch as records of action currents either of many muscle or of many nerve fibers present irregular waves due to the combined asynchronous activity of many individual units some such method as that of Travis and Hunter is abso-

lutely necessary if we are to have any reliable quantitative treatment of the action currents. Even if action currents from single units consist of repeating waves the voltage-frequency method could be used to good advantage. However, because very few pictures published of such action currents present absolutely periodic waves this method seems almost as necessary for the study of the electrical activity of a single unit as of many functional units. This is particularly true since the method of Fourier analysis can not be applied to waves unless the waves are absolutely periodic in form, frequency and amplitude. Such periodicity is the rare exception even in action currents from single units. Thus the statement of Davis, Forbes and Garceau that a "Fourier analysis may be applied to the oscillograms of the individual impulses" is not generally true.

LEE EDWARD TRAVIS
THEODORE A. HUNTER

STATE UNIVERSITY OF IOWA

SCIENTIFIC BOOKS

The Wisdom of the Body. By WALTER B. CANNON, M.D., Sc.D., LL.D. W. W. Norton & Co., Inc., 1932, pp. 1-312.

THIS volume reads as though a college professor, with a mind rich in knowledge based on a lifetime of fruitful research in the laboratory, had set himself down upon his piazza in the cool evenings of the summer time and there recorded in simple but glowing language his thoughts concerning the facts and problems which had been uncovered by his life's work and were vibrating in his mind at the time. As to the language employed one might quote the fine description of the storage of water in the skin and in the muscles: "The entrance of water into these storage places appears to be a sort of *inundation*. I have already likened the lymph spaces to a swamp in which fluid stagnates. The analogy is implied also in the word *inundation*. We may think of the tissue spaces as being a sort of bog into which water soaks when the supply is bountiful and from which the water seeps back into the distributing system (the blood vessels) when the supply is meager." The use of lucid language of this sort justifies the author's expectation that the volume will be of interest not only to biologists but to the general reader as well. The book presents in comprehensible language the exquisitely sensitive regulatory mechanisms which maintain the units of the body in a state of nearly balanced equilibrium. Cannon terms this state "homeostasis," meaning thereby a condition which is relatively constant. The description of how homeo-

stasis is maintained is accomplished without resort to complicated mathematical formulae but in straightforward talk of the obvious results of physiological experimentation.

In this manner the safeguarding of the fluid matrix is considered, and the homeostasis of the blood in regard to its content of water, of salt, of glucose, of protein, of fat, of calcium and of its neutrality of reaction. Also the regulation of body temperature is described. With great precision Cannon has revealed that the first action of exposure to cold is to cause a discharge of epinephrin into the circulation. This he determined by giving ice water to a cat the nerves of whose heart had been cut. Such a heart is very sensitive to an increased supply of epinephrin in the circulating blood, and an experimental application of cold, either internally as above or externally, resulted in a rapid increase in the heart rate. It is a matter of knowledge which we owe especially to Boothby that epinephrin increases the heat production, or in other words exerts a calorogenic action. In another place Cannon has called this increase of heat production through liberation of epinephrin from the adrenal gland the fine adjustment in the maintenance of body temperature, whereas shivering constitutes the coarse adjustment by which the heat production is increased to compensate for heat loss at the surface. The two factors, which were first clearly differentiated by Cannon, constitute the entity which Rubner called the "chemical regulation of body temperature" in contrast with the protection offered by

the distribution of blood and the evaporation of water which constitute the "physical regulation of body temperature." Although Cannon has quoted generously from recent contemporaneous literature, the critic may perhaps be pardoned for asking why, of the older authorities, Claude Bernard alone should be the scientist freely cited. Perhaps, however, the charm of the book lies in the fact that it represents enticingly the view-point of a laboratory worker of rich experience speaking out of that fulness of personal knowledge, a method which compels interest in the subject and regard for the author.

In a final chapter Cannon discusses the possibility of the establishment of a "steady state" in the social and economic world. In this he follows the example of Aristotle in a celebrated passage which began, "The animal organism is to be conceived after the similitude of a well-governed commonwealth." Cannon suggests that the steady state of the fluid matrix of the animal organism indicates that the social organism should be provided with specially organized control over the processes of commerce. This would include the power to limit the production of goods so as to adjust the supply reasonably to the demand, the power to lay aside stores of goods and stores of wages and the power to arrange emergency employment. All these in a measure are represented as factors of safety in the human body. Perhaps one might suggest another analogy, which is, the fact that a human being, through undernutrition, may be brought to a level of maintenance of two thirds the quantity of food necessary for the normally nourished, even though at some loss of the sense of personal well-being. At a time when wheat is selling at the farm at 25 cents a bushel, in contrast with \$2.20 during the war, it does not seem right that war-time wages should be practically guaranteed to railroad workers. Perhaps in times of economic distress the political leaders of Aristotle's "well-governed commonwealth" would have been so wise and so free from vote-getting ambition as to have decreed a reduction in railroad wages suggested by the 30 per cent. physiologically possible reduction in food calories, to the end that other wage-earners might be continuously

employed. Into such seemingly fantastic analogies contemplation of the "Wisdom of the Body" leads us.

GRAHAM LUSK

The Universe Unfolding, By ROBERT H. BAKER, x+140 pages. The Williams and Wilkins Company, Baltimore, 1932. \$1.00.

THIS is an excellent book to be one of the volumes of the Century of Progress Series. The originality shown in the manner of presenting the astronomical facts will appeal alike to those who already know these facts, and to those who do not. It is a long way from the flat circular plane of the Greek's earth, over which bends the solid stationary dome of the sky, to the universe of galaxies and supergalaxies lying millions of light years beyond the solar system. However, the 140 pages of the book do cover this distance in a very satisfactory manner, and among these pages will be found the answers to many questions frequently asked by people in general about the modern methods of investigating the astronomical universe. This book can hardly fail to give any reader a better understanding and a greater interest in "the vast universe around us and the mysterious mind of man."

The first chapter tells of the universe as man in the past understood it, first according to the Ptolemaic system with the stationary earth at the center, and then according to the system of Copernicus with a central sun about which the earth and the other planets revolve. The second chapter takes up the story of the investigation of the sidereal system from the star gauges of Herschel to the statistical studies of Kapteyn, and then on to the work of the present day which has disclosed millions of vast stellar systems. The remaining chapters are devoted to the modern methods of investigating the structure of the universe. These describe the various methods of attack on this problem and tell the amount of success achieved by each method. The last chapter brings this interesting account up to the most recent discovery, which is that the exterior galaxies appear to have huge velocities of recession with respect to our own galactic system.

IDA BARNEY

YALE UNIVERSITY OBSERVATORY

SOCIETIES AND ACADEMIES

THE IOWA ACADEMY OF SCIENCE

THE forty-sixth annual meeting of the Iowa Academy of Science was held with Iowa State Teachers College at Cedar Falls on April 29 and 30, 1932, with 245 members and visitors in registered attendance.

The presidential address, "Our Underground Geology," was presented by Dr. James H. Lees, of the

Iowa Geological Survey. Other papers of general interest were: "The Oxidation of Citric Acid," by Adrian S. Kuyper, of Iowa State University; "Some Observations on Spectral Color Discrimination," by Le Roy D. Weld, of Coe College; "The Effect of Pre-school Attendance upon Intelligence Quotient," by Dr. Beth L. Wellman, of the Iowa Child Welfare Research Station; "The Iowa Conservation Plan," by

J. R. Crane, of the Iowa Fish and Game Commission. The annual academy lecture was presented by Dr. L. L. Thurstone, of the University of Chicago, on "The Measurements of Social Attitudes."

The Junior Academy of Science of Iowa met with the Iowa Academy at this time for its organization meeting. The following officers were elected: *President*, Henry Estabrooks, Dubuque High School; *vice-president*, Dwight Thompson, Des Moines; *secretary*, Genevieve Ostergaard, of Cedar Falls; and *treasurer*, Walter Brown, of Cedar Falls.

The officers of the academy and the chairmen of its sections for the forthcoming year will be: *President*, H. E. Jaques, Iowa Wesleyan College; *vice-president*, J. E. Guthrie, Iowa State College; *treasurer*, W. F. Loehwing, Iowa State University; *secretary and American Association for the Advancement of Science representative*, Joseph C. Gilman, Iowa State College; *editor*, Mrs. F. W. Nichols, Ames; *bacteriology and botany*, C. H. Werkman, Iowa State College; *chemistry, general and physical*, W. B. Zuker, Dubuque; *chemistry, organic and biological*, L. W. Sherman, Grinnell College; *geology*, J. E. Smith, Iowa State College; *mathematics*, L. M. Coffin, Coe College; *physics*, H. J. Plagge, Iowa State College; *psychology*, L. C. Douglass, Grinnell College; and *zoology*, E. R. Becker, Iowa State College.

The Academy convened in eight sections for the presentation of 133 papers of special interest. The retiring section chairmen made the following reports of their respective meetings.

Bacteriology and Botany: G. W. MARTIN, *chairman*. Of the thirty-one papers in the bacteriology-botany section eleven were concerned with bacteria and fungi in various relations and the remainder with botanical studies ranging from papers on mosses and ferns to those in the fields of morphology, cytology and taxonomy. An important feature of the program was the conference on the teaching of botany held on Friday morning, which was largely attended. At the close it was voted to continue this phase of the meeting another year.

Chemistry: H. GREGG SMITH, *Chairman*. Among the papers presented before the organic-biological section were the following: "Vanillin Substitution Products with Acetophenone," by Gundy and Raiford; "Condensation of Furan, and Furan Arsenicals," by Henry Gilman and his students; "Reaction of Chloroamines with Zinc Alkyls," by Coleman and Andersen; and two papers on "Phenolic Ketimines," by Culbertson and his students. The biological papers included: "A Statistical Analysis of the Growth of Rats in the Stock Colony of the Foods

and Nutrition Department of Iowa State College during the Years 1928-31," by Gladys Timson, Pearl P. Swanson and P. Mabel Nelson; "Vegetable Lecithin as an Antioxidant," by Kochenderfer and H. G. Smith; "A Study of Methods for the Determination of Reducing Sugar in Bacteriological Media," by McCreary and H. G. Smith. Of special interest was a report on "The Rôle of Copper in Hemoglobin Regeneration," by Keil and V. E. Nelson, in which the importance of traces of copper was emphasized. The joint dinner of all the chemists was addressed by Drs. Raiford, Knight, Bartow and Petersen.

Geology: E. J. CABLE, *Chairman*. The Geology Section of the Iowa Academy of Science which met at Cedar Falls, Iowa, on April 29 and 30, had a most interesting and profitable meeting. Papers representing stratigraphic, paleontologic and Pleistocene geology were ably presented and discussed. Some of the more outstanding papers were, "Interpretation of the Relationships of Iowan Drift," "The Peorian Loess," and "The Wisconsin Drift from Recent Studies in Iowa and Illinois"; "The Upper Devonian Beds in Iowa County," "Sedimentation of the Cedar Valley Limestone"; "The Cedar Valley Limestone at Gloria and Waterloo, Iowa"; "Interglacial Mammalian Remains"; "The Story-Hamilton Artesian Area"; "Discussion of the Section of the United States from Lake Superior in Wisconsin to Oklahoma," prepared by the Kansas State Geological Society; "Ice Caves," and several other papers of less importance.

Physics: T. C. POULTER, *Chairman*. A group of twenty-one papers, covering a number of very interesting topics was presented and discussed in the Physics Section meeting of the Iowa Academy of Science. Several papers were presented in the Friday afternoon session followed by the Physics dinner at the Tip Top Tavern. Following the dinner a very interesting and inspiring lecture was given by Dr. C. J. Lapp, of the Department of Physics, University of Iowa, on "The Structure of the Nucleus." This lecture was well illustrated by lantern slides. A vast amount of recent information was presented on the most fascinating topic in modern physics. The remainder of the papers were presented at the Saturday morning session, following which Dr. H. G. Plagge, of Iowa State College, was elected chairman of the Physics Section for the coming year.

Psychology: THOMAS F. VANCE, *Chairman*. Among the eight sections of the Iowa Academy of Science, Psychology ranked third in the number of papers presented at the 1932 meeting. The eighteen papers may be classified as follows: General 3, educational 7, child 3, tests and measurements 4, and industrial 1. Space does not permit the listing of the papers pre-

sented but they will be published either in full or by abstract in the "Proceedings" of the academy. This year the academy's evening lecture was in the field of psychology, Dr. L. L. Thurstone being the speaker on the subject, "The Measurement of Social Atti-

tudes." Dr. Thurstone also spoke to the psychologists assembled at dinner on the subject, "Modern Psychophysics."

JOSEPH C. GILMAN,
Secretary

SCIENTIFIC APPARATUS AND LABORATORY METHODS

A NEW HYDROGEN ELECTRODE AND APPARATUS FOR THE DETERMINATION OF pH

It is known that, in order to measure the pH of liquids containing CO_2 in solution, such as blood, serum, tyrode solution, etc., it is necessary to prevent the escape of CO_2 which would result in an erroneous reading. Furthermore, Hasselbach and Clark have shown that it was necessary, in order to obtain reliable and stable measurements, to keep the platinized-platinum electrode successively in contact with the liquid and with the atmosphere of hydrogen. This is obtained, in the well known Clark's electrode, by shaking the vessel by means of an electric motor. This method can be considered as standard and yields excellent results. However, it requires rather large quantities of serum or blood (6 cc), and the time necessary to reach the equilibrium is long. Besides, the apparatus, entirely made of glass, incorporates four glass stopcocks, rubber tubing, clamp, and does not lend itself to an easy temperature control.

We have recently worked out an hydrogen electrode in which the equilibrium is reached in about one minute, for ordinary solutions, with less than one cc of liquid. The principle is different from that of Clark's electrode as it is based on the permanent rotation of a tilted electrode in the shape of a disk, one half of which dips in the liquid, the other half being in the hydrogen. During its rotation, a thin layer of liquid carried by the disk is constantly brought in contact with H_2 and, as the rate of rotation may be as high as 500 revolutions a minute, the saturation takes place in a very short time. The readings are taken while the electrode is in motion, and are very constant. It is useless to say that all sorts of shapes can be used for the platinum electrode: spiral, screw propeller, etc. Of course, a proper technique is used to fill the cup with the serum and introduce H_2 with the minimum possible loss of CO_2 . (Fig. 1). Practically, a glass syringe is used: the platinum disk is fixed to the piston, and the liquid-liquid junction is established through a capillary tube. One or two hydrogen bubbles are sufficient.

In order to simplify the handling and to reduce the chances of breakage, we have the whole apparatus (hydrogen and calomel electrodes stand) made of metal (see Figs. 2 and 3), the only glass parts being

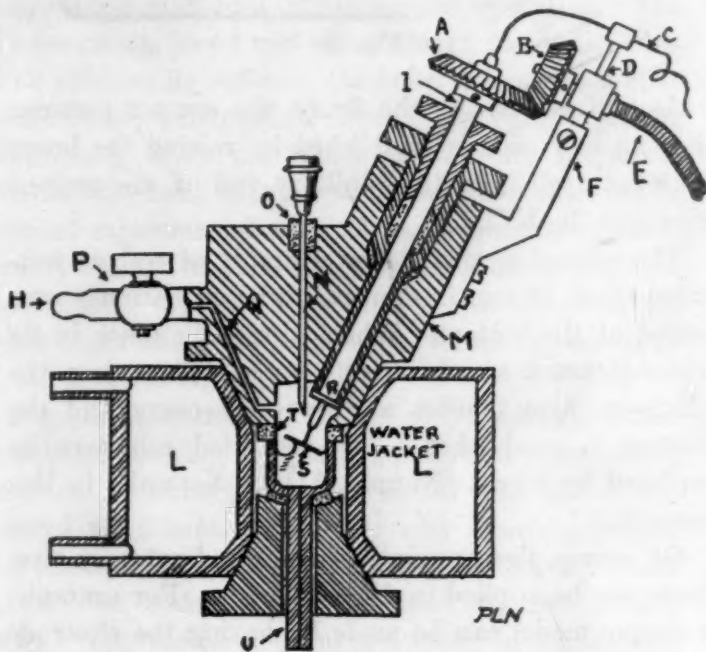


FIG. 1

the syringe and the calomel electrode. Both hydrogen and calomel electrodes are water-jacketed and may be taken apart in a few seconds. No glass stopcocks, nor expensive glass parts are used. No troublesome diffusion was observed in one hour.



FIG. 2

When this instrument is used to determine the pH of ordinary solutions, the rotatory electrode is no longer absolutely necessary. It may then be replaced—and the change is done instantaneously—by a simple platinum tube, through which the hydrogen is allowed to bubble gently in the liquid. In this way,

the equilibrium is also attained in an amazingly short time, and the readings take place while the bubbling goes on.

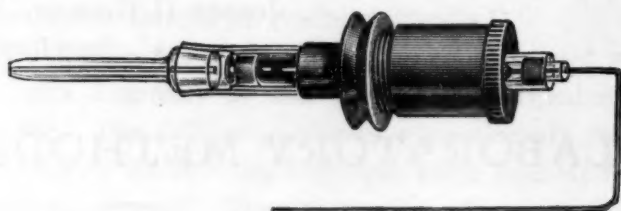


FIG. 3

As will be seen on the figure, the contact between the two half cells is established by raising the lower (calomel) cell until the capillary end of the syringe dips into the KCl.

The calomel element consists simply of a short test-tube, about 18 mm in diameter, with a platinum wire sealed at the bottom. When slipped in place in its water-jacketed stand, it rests on a rubber ring, the platinum wire touches a drop of mercury and the contact is established. The saturated cell may be replaced by others (Normal, 1/10th Normal), in two seconds.

Of course, the principle of the tilted rotatory electrode can be applied in different ways. For example, a simple model can be made by having the electrode and the vessel containing the liquid and H_2 connected through a rubber stopper, the whole being then rotated around its axis at such an angle that will allow the liquid to cover about one half of the electrode.

This apparatus, whether used with the simple tubular electrode for ordinary solutions, or with its tilted rotatory electrode, lends itself particularly well to measurements in series, as the setting up, filling of the syringe, saturating with H_2 , and measuring the E.M.F. never takes more than five minutes with ordinary solutions.

P. LECOMTE DU NOÛY

INSTITUT PASTEUR

A METHOD OF RELACQUERING THE STEMS OF LIVINGSTON ATMOMETER BULBS¹

In the course of certain ecological work in the Hawaiian Islands, it was found that the lacquer on the stems of some Livingston atmometer bulbs began to peel off after about six months' service in the field, and the writer was requested to make repairs on these bulbs. The exact cause of this peeling was not determined, but it was believed to be due to overliberal use of alcohol, used to sponge off the bulbs to prevent algal growth.

Attempts to relacquer with ordinary white shellac proved quite unsuccessful, but after several trials with various mixtures, the following proved very satisfactory.

To 100 cc of prepared white shellac (already dissolved in alcohol), add 30 to 35 cc of absolute alcohol, and shake. To this stock add 30 to 35 cc of fresh Canada Balsam (not the histologist's preparation dissolved in xylol, but the fresh liquid balsam as purchased from a druggist) and mix well.

The bulbs to be repaired are then thoroughly dried out, and all old lacquer removed from the stems with a razor blade. In effecting this removal some care must be used not to damage the surface of the stem more than necessary, since such abraded patches are very absorbent and difficult to relacquer.

The stems are then painted with a thin coat of the above mixture and allowed to dry in a warm room, but *not in an oven*, and when dry are given a second or even a third coat, until when dry, the whole stem has a shiny and polished appearance.

SUMMARY

A method of relacquering the stems of Livingston atmometer bulbs by the use of a mixture of white shellac and Canada Balsam is outlined, together with certain precautions to be observed in the process.

JOHN STANLEY

SPECIAL ARTICLES

THE APPARENT PREPOTENT FUNCTION OF THE ADRENAL GLANDS¹

ACCUMULATING evidence indicates the direction in which solution of the adrenal enigma may be found. The Harvard school of workers led by Cannon have in the last decade delivered a veritable broadside of reports on medulliadrenal activities, and almost universal support of their findings has been forthcoming. Emergency functions which are subserved

¹ Reported *in extenso* at a meeting of the University of Virginia Medical Society, January 18, 1932.

through medullary agency appear to be established.² Observations by Cori and his colleagues direct attention to the importance of carbohydrate changes wrought particularly through the influence of adrenalin.³ Early work by one of us on the adrenal

¹ Published with the approval of the director as Miscellaneous Paper No. 12 of the Experiment Station of the Association of Hawaiian Pineapple Cannery, University of Hawaii.

² W. B. Cannon, "Bodily Changes in Pain, Hunger, Fear, and Rage," 1929.

³ C. F. Cori, *Physiol. Rev.*, 11: 143, 1931.

medulla has related this tissue to the metabolism of carbohydrates.⁴

The recently devised methods of preparing effective extracts of the adrenal cortex have opened new approaches and allowed rapid advances in a phase of the subject generally acknowledged to be most difficult. For this development great credit is due to Swingle and Pfiffner⁵ and to Hartman and his colleagues.⁶

Three years ago investigations were taken up in this laboratory on the nature of cortico-adrenal activity. Preliminary results strongly suggested a relationship of the adrenal cortex to carbohydrate metabolism in the organism. Further experiments in this⁷ and other laboratories have indicated, however, that possibly protein metabolism and also renal and sexual activities may be governed by the cortical tissues.

Workers at Princeton and Johns Hopkins⁸ have attributed considerable importance to the marked changes in renal secretion which follow adrenalectomy and the amelioration which is brought about by the administration of cortico-adrenal extract. The augmentation of blood urea in adrenal insufficiency, and the reduction effected by the extract, are also believed to be of outstanding significance. In a previous report⁷ we have pointed out that such effects are probably indirect or secondary to more fundamental changes. Renal activity appears to follow the general and circulatory conditions in adrenal insufficiency. Animals which have died from adrenal deprivation do not show any significant alteration in kidney tissue; frequently, indeed, no pathological change has been observed in our experiments.

It can hardly be considered that the accumulation of unutilizable protein end-products in the body or the diminution in kidney secretion represent pre-eminently critical conditions in the adrenalectomized animal. Nor can it reasonably be entertained, furthermore, that precocious sexual developments which are observed to be brought about by cortical extract,⁹ interestingly significant though they may be, reflect the primary activity of the adrenal cortex. That the effects on the sexual organs probably indicate the activity of a hormone of a second-class order, which is present in the crude extract, has been postulated. The essentially important cortical function must evidently be sought in other directions.

Apparently convincing testimony of the profound and possibly primary involvement of the adrenal cortex in the regulation of carbohydrate metabolism is now briefly presented. Cortico-adrenal extract prepared in this laboratory according to the method of Swingle and Pfiffner⁵ has been employed.

Adrenalectomized animals (cats) have been found to suffer progressively severe derangements in carbohydrate metabolism following the operation. The glucose in the blood and the glycogen in the liver become profoundly reduced, the latter sometimes almost to the disappearing point. Muscle glycogen is greatly diminished, while the blood lactates are increased. The carbohydrate changes which we have observed in cases of experimental adrenal insufficiency are revolutionary enough in themselves to bring about death of the animal. Serious reductions which occur in the blood sugar and hepatic glycogen values appear to be of the greatest significance.

The administration of extract of the adrenal cortex to animals showing symptoms of adrenal insufficiency produces a remarkable reversal of the above disordered conditions. The liver and muscle glycogen and blood sugar levels are increased and the lactic acid values are concurrently decreased to the normal limits. The chemical changes appear in coincidence with the return of the animal to normal activity, *i.e.*, in the few hours following intraperitoneal injection of the extract.

Adrenalectomized animals which are obviously in a terminal dying condition, and which are known to be suffering crucially from glycogen depletion, may be completely recovered by the extract. Adrenalin given in dilution equal to that usually found in the cortico-adrenal extract used does not bring about similar restoration of the animal or such noteworthy carbohydrate changes.

The table herewith presents in summary our experimental results. The average muscle and liver glycogen values of the treated animals (series IV) are increased about threefold and twentyfold, respectively. It may be noted, in contrast to the values found in untreated adrenalectomized animals (series II).

Comparison has also been made of the effects of glucose injections in normal and adrenalectomized cats. In such experiments, large amounts of glycogen were found to be stored by unoperated animals, while those without adrenals showed relatively small glycogen changes from the previously observed low levels.

It is recognized that all theories of adrenal function are at present inadequate. The emergency theory offers an admirable interpretation of the mode of medulladrenal activity, but knowledge of cortical function has been shrouded in conjecture up to the present

⁴ S. W. Britton, *Amer. Jour. Physiol.*, 74: 291, 1925; *Physiol. Rev.*, 10: 617, 1930.

⁵ W. W. Swingle and J. J. Pfiffner, *Amer. Jour. Physiol.*, 96: 153, 1931.

⁶ F. A. Hartman, K. A. Brownell and W. E. Hartman, *Amer. Jour. Physiol.*, 95: 670, 1930.

⁷ S. W. Britton *et al.*, *Amer. Jour. Physiol.*, 99: 9, 15, 33, 44, 1931.

⁸ G. A. Harrop *et al.*, *Anat. Record*, 51: 39, 1931.

⁹ E. L. Corey and S. W. Britton, *Amer. Jour. Physiol.*, 99: 33, 1931.

TABLE SHOWING GLUCOSE, GLYCOGEN, AND LACTIC ACID
LEVELS UNDER VARIOUS EXPERIMENTAL
CONDITIONS

Series No.	No. cats used	Experimental conditions	Muscle glycogen average per cent.	Liver glycogen average per cent.	Blood sugar average per cent.	Blood lactic acid average per cent.
I	5	Normal, fasted 48 hours432	1.480	.112	.025
II	9	Adrenalectomized, untreated208	0.067	.048	.038
III	5	Adrenalectomized, adrenalin treated392	0.276	.051	.031
IV	8	Adrenalectomized, extract treated585	1.305	.097	.026
V	6	Normal, fasted 48 hours, glucose treated336	2.120	.137	.025
VI	5	Adrenalectomized, glucose treated398	0.275	.206	.035

time. That the cortex in contrast to the medulla is of premier importance in the bodily economy has, nevertheless, been long appreciated.

The adrenal glands are indispensable in the maintenance of life processes. Considering their size they are possibly the most important chemical factories in the body. Extirpation of the organs brings about death in a few days. After pituitary, thyroid or parathyroid removal life may be maintained for many weeks or months, or even indefinitely in some cases. The remarkably rapid dissolution following adrenalectomy is due specifically to cortical loss.

Even in the severest conditions of inanition and exposure of animals to cold, in death from insulin or strychnine convulsions, and in experimental diabetes, the hepatic and muscle glycogen values are not often found to be reduced beyond the low levels which we have observed in adrenal insufficiency. The muscle glycogen and blood glucose in hepatectomy are not depleted more thoroughly than in the case of animals dying from adrenal extirpation. And in hepatectomy as well as pancreatectomy death is admitted to be due primarily to carbohydrate deficiency.

The results given herewith indicate that the severity of the carbohydrate changes in adrenalectomized animals is fully sufficient to produce death. This eventuality is readily averted by cortico-adrenal extract administration, which results in rapid restoration of the normal blood glucose and liver and muscle glycogen values. A serious incompetence in storing injected glucose has also been noted in animals with-

out adrenal glands. The cortex is indispensably important in maintaining, in cooperation with other organs, the normal metabolism of carbohydrates. This apparently represents the prepotent function of the adrenal cortex in the organism.

Possibly the primary defect in adrenalectomy is to be found in failure to store liver glycogen. Adrenal insufficiency may perhaps be considered in synonymy with glycogen insufficiency.

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SOME EFFECTS OF OVARIECTOMY UPON BREEDING FEMALES

It has previously been observed¹ that the secretions of the ovaries play an important part in the preparation of the mammary tissue of mice for the inception of the cancerous condition.

In a closely inbred strain of mice with a high incidence of breast cancer, it has been found that the age at which the appearance of the tumors was first noted follows a very regular unimodal curve which starts at four months, has its peak at eleven months and extends to the twenty-second month. The lower range of the standard deviation from the mean (11.6) of this curve falls in the 8th month. From this it is evident that the great majority (80-90 per cent.) of the females which are destined to develop cancer of the breast will do so between the seventh and fifteenth months.

The present experiment was conducted in an attempt to determine whether or not the high incidence of tumor in this strain is in any way controlled by ovarian activity.

Breeding females were separated from the males at seven months of age and were ovariectomized. They were then allowed to grow old under the same conditions as the control breeders. An equal number of breeding females were separated from the males at this same age and kept under similar conditions without operation, as controls.

There were then three distinct classes of animals in the experiment:

- (1) Normal breeding females.
- (2) Ovariectomized females which had been used as breeders for seven months.
- (3) Females that were used as breeders for seven months and then separated from the males.

In the first class there were 1,938 females which

¹ Porter Fellow of the American Physiological Society.

¹ W. S. Murray, "Ovarian Secretion and Tumor Incidence," *The Journal of Cancer Research*, Vol. xii, No. 1, March, 1928.

lived to be over seven months of age. Of these, 1,275, or 65 per cent., died of cancer of the breast.

In the second class there were 195 animals. Of these 78, or 40 per cent., died of cancer.

In the third class there were 198 animals, 140 of which, or 70 per cent., died of cancer.

It is evident from the above that ovariectomy of breeding females at seven months reduces, markedly, the incidence of mammary cancer.

TABLE I
EXPECTATION OF LIFE

Age in months	Breeding females	Control females	Operated females
7-8	4.4	4.6	6.2
8-9	3.5	4.1	5.8
9-10	3.0	3.3	5.6
10-11	2.6	2.9	5.5
11-12	2.3	2.4	5.7
12-13	2.1	2.0	5.8
13-14	1.9	1.6	6.0
14-15	1.8	1.5	5.8
15-16	1.7	1.5	5.6
16-17	1.5	1.3	4.8
17-18	1.3	1.1	4.3
18-19	1.3	.7	4.5
19-20	1.2	.5	4.2
20-21	1.0		3.7
21-22			3.5
22-23	1.0		3.4
23-24			3.3
24-25			3.3
25-26			3.0
26-27			2.0
27-28			2.5
28-29			1.5
29-30			1.0
30-31			.5

If the expectation of life² (in months) is computed for the breeding females of this stock, regardless of the cause of death (Table I, Column 1), it is found to be 4.4 at seven months and falls in a steady curve to 1 when the mice are twenty-two months old.

If the expectation for the control females is computed in the same way, it is found that the curve closely approximates that of the breeding females but ends two months earlier.

The expectation curve for the operated animals is markedly different. Starting at 6.2 months, it falls off for four months, rises again until it reaches six at the thirteenth month, and then ranges gradually downward to .5 at the thirtieth month. This indicates that ovariectomy of breeding females during the seventh month not only prolongs the lives of some indi-

viduals in a marked degree but delays death among them so generally that at 17 months they have the same (or greater) expectation of life as do the breeding females at 7 months.

It appears from these data that ovariectomy of breeding females approaching the cancer age protects them to some extent against as early death as they would have had without operation.

That it also protects them in some degree against cancer of the breast may be seen from Table II.

TABLE II
PER CENT. OF THOSE DYING IN EACH AGE PERIOD,
WHICH HAD MAMMARY CANCER

Age in months	Breeding females	Control females	Operated females
7-8	34	25	22
8-9	43	64	52
9-10	56	73	38
10-11	64	100	38
11-12	72	69	52
12-13	83	80	73
13-14	84	85	40
14-15	77	75	50
15-16	77	67	50
16-17	91	100	40
17-18	91	50	27
18-19	93	0	60
19-20	83		50
20-21	75		60
21-22			20
22-23	100		0
23-24			0
24-25			0
25-26			0
26-27			0
27-28			0
28-29			0
29-30			0

Here it is demonstrated that the percentage of those dying of cancer in each age period is appreciably higher in the breeding females and controls. It is shown that all the ovariectomized females in this experiment which live to be more than 22 months old are completely free from cancer.

To summarize: The influence of the ovary on the incidence of mammary cancer is, in this stock of mice, clearly established. It is sufficiently striking so that it may be demonstrated by removal of the ovary from breeding females seven months old. The removal of the ovaries greatly increases the expectation of life and decreases the incidence of mammary cancer.

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² Raymond Pearl, "Medical Biometry and Statistics," W. B. Saunders Co., Philadelphia, 1930.

GROWING COTTON AND OTHER CROP PLANTS WITH AMMONIUM NITROGEN¹

WILLIS and Rankin² grew cotton seedlings in soil in which had been added cottonseed meal in a concentration equivalent to 16 pounds of nitrogen per acre. Associated with the application of cottonseed meal, there occurred definite injury to the roots. They attributed this injury to "ammonia toxicity." This interpretation of their results accompanied by considerable publicity has led to the erroneous idea that ammonium fertilizers are toxic to cotton plants. Their results do not warrant such a generalization. These results were apparently obtained under conditions where the soil buffer system was inadequate. They added calcium sulphate and the cotton seedlings were not injured. Calcium sulphate may have acted as an adsorbent, and, thereby, prevented the hydrogen-ion concentration from becoming too high or too low for the welfare of seedling roots.

The conclusion that ammonia is toxic is not in harmony with results secured by Tiedjens and Robbins³. They grew various plants with sulphate of ammonia and ammonium hydroxide at pH values of 7-8.8; tomato and soy-beans were supplied with sulphate of ammonia in sand cultures, and good growth was obtained, but the plants exhibited even more luxuriant growth when supplied with ammonium hydroxide. Growth was comparable to that of good field-grown plants, and equal or superior to that of others in sand cultures, which received all their nitrogen from calcium nitrate.

Cottonseed meal, as employed by Willis and Rankin, for some reason produced injury to cotton seedlings. The interpretation of these workers would imply that the cotton plant is peculiarly sensitive to extremely low concentrations of ammonia nitrogen. Since the publication of their data, cotton has been grown by the author in sand cultures from the seedling stage to the opening of the bolls, with sulphate of ammonia, ammonium hydroxide and calcium nitrate, respectively. Ammonium hydroxide was supplied in a complete nutrient solution at pH 8. At no time was there any indication of injury to the plants, even though there was a perceptible odor of ammonia coming from the ammonium cultures. At the present time, these plants are five feet high, profusely branched, and producing flowers which have resulted in numerous bolls, which are beginning to open. If there is any

superiority between the two forms of nitrogen, it is in favor of the ammonia cultures.

The concentration of nitrogen as ammonia in these cultures was higher than that of the total nitrogen in the cottonseed meal, which was employed by Willis and Rankin,² and which they state was toxic to cotton plants on account of the free ammonia liberated.

Tomato, soy-bean and cotton can adsorb ammonia over a wide range⁴ of pH (3.5-8.0), but these plants will not assimilate the ammonia³ (synthesize simple proteins from ammonia), unless, when supplied to the plants, the pH of the nutrient solution is above 6. When conditions are unfavorable for assimilation of ammonium nitrogen, it may accumulate in the plant to a considerable concentration. It does not injure the plant any more than does the accumulation of nitrate nitrogen. Nitrates may also accumulate in the plant in large quantities, when reductase activity⁵ is limited.

If a nutrient solution containing nitrogen as ammonium only is supplied to a cotton plant at pH 3.5, no perceptible growth is made, even though some ammonia is absorbed. If the pH is raised to 7.5 or 8, perceptible growth takes place in 48 hours.

Holly, Pickett and Dubin⁶ grew cotton in solution cultures in which their solutions were supplied to the plants at pH 6. They report a larger volume of growth for the nitrate plants. The appearance of the ammonium supplied plants resembled those grown by the author at pH 6.5. This pH value was found to be too low in sand cultures for maximum elaboration of ammonium nitrogen in cotton.

The fact that injury did not result from the accumulated ammonia and that growth took place soon after shifting to the higher pH seems sufficient proof that ammonia is not more toxic than other nutrients. The results of Willis and Rankins are valuable in that they show the importance of a buffer system in sandy soils where incomplete fertilizers are used. The generalization that ammonia is toxic to plant growth, under good cultural conditions, is no longer tenable.⁴

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